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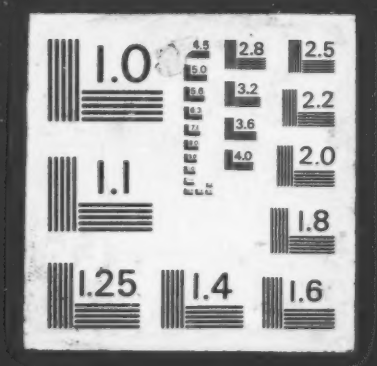

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PUBLICATION

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TOXICOLOGY PROGRAM
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DDT and DDE Content of Complete Prepared Meals

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IN EVALUATING the health hazard of pesticides to man it is important to know the total daily intake of these agents. For the general population who have no specific environmental or occupational contact with pesticides, the major source of absorption is the intake of small residues of these compounds which occur in the diet.

An earlier study was published in 1954 [1] indicating the average daily intake of DDT and DDE in prepared meals at that time. This paper reports a study which was carried out to determine the present level of DDT and DDE residues in complete meals. Also included are a few tests to determine the comparative DDT and DDE contents of some selected "health foods" and of similar items purchased in an ordinary grocery store.

This paper describes work which is a component part of a more comprehensive study. The complete project involves determination of DDT and DDE storage levels in body fat in the general population and in specific environmental and occupational groups, measurement of DDA excretion levels in these same population subdivisions, and determination of DDT and DDE excretion in milk by nursing mothers. These surveys have been correlated by obtaining as many of the samples as possible from, or in relation to, the same individual. The results of other segments of the study will be published separately.

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Materials and Methods

A total of 29 complete meals were analyzed. This number included 12 restaurant and 17 household meals. A total of 177 individual food items were tested.

Since the results reported were to be compared with those of the earlier survey carried out at this laboratory,[1] materials and methods were kept as nearly the same as possible. Briefly, the procedure involved collecting the individual food items separately in chemically clean glassware directly from the kitchen of the restaurant or home. The individual items were weighed after discarding inedible portions. The foods were extracted with acetone in a Waring blender and filtered. The filter cake was then extracted with carbon tetrachloride in a Soxhlet extractor. The two extracts were combined and concentrated for analysis. Prior to the final colorimetric analysis, the combined extracts were passed through a Davidow column for removing interfering fats and pigments.

Ten selected foods items were purchased from two different "health food" stores. These specific foods were not stated to be pesticide-free although the advertising for the stores included the general claim of freedom from sprays for the merchandise. Corresponding items were purchased at an ordinary grocery store. Both series of food items were tested for DDT and DDE residues.

The DDT and DDE determinations were carried out by the Schechter-Haller spectrophotometric method [2] as modified by Mattson.[3] In order to determine the extent of loss of detectable amounts of DDT and DDE during testing, known quantities of the compounds were added to representative food items; then the extraction and determination procedures were carried out. The recoveries ranged from 43% to 89% (mean, 68%) for DDT and from 62% to 96% (mean, 79%) for DDE.

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TABLE 1.—*DDT and DDE Content of Restaurant and Household Meals*

Meal	Total Weight of Meal (Including Beverage) (gm)	Total (mg) DDT	DDE	Total (as DDT)	DDE (%)
Morning:					
1-RM *	556	<0.005	0.009	0.010	90
2-RM	845	0.015	0.015	0.032	52
3-RM	1,125	0.004	0.022	0.029	84
4-RM	577	0.011	0.013	0.025	58
5-HM †	462	<0.005	<0.005	<0.005	—
6-HM	495	0.056	0.125	0.195	71
7-HM	333	0.017	0.005	0.023	22
8-HM	605	1.160	0.730	1.970	41
9-HM	1,463	<0.005	<0.005	<0.005	—
10-HM	494	<0.005	<0.005	<0.005	—
Mean	606	0.126	0.092	0.228	45
Noon:					
11-RM	723	0.020	0.023	0.045	56
12-RM	743	0.034	0.024	0.061	44
13-RM	465	<0.005	<0.005	<0.005	—
14-RM	603	0.014	0.013	0.028	50
15-HM	594	0.139	0.042	0.186	25
16-HM	588	0.031	0.011	0.043	28
17-HM	630	0.005	<0.005	0.005	—
18-HM	474	<0.005	<0.005	<0.005	—
19-HM	913	0.260	0.024	0.287	9
Mean	637	0.056	0.015	0.073	23
Evening:					
20-RM	817	0.012	0.034	0.050	76
21-RM	806	0.019	0.016	0.037	49
22-RM	409	<0.005	<0.005	<0.005	—
23-RM	890	0.014	0.006	0.024	42
24-HM	573	0.032	0.005	0.038	16
25-HM	1,382	0.048	0.039	0.091	47
26-HM	672	0.014	0.033	0.051	73
27-HM	857	0.010	<0.005	0.010	—
28-HM	725	<0.005	<0 005	<0.005	—
29 HM	840	0.023	0.013	0.037	38
Mean	804	0.017	0.015	0.034	50
Mean daily total	2,137	0.199	0.122	0.335	40

* Restaurant meal.
† Household meal.

These values may be compared with recoveries of DDT and DDE carried through the entire procedure with no foods involved; these recoveries ranged from 77% to 95% (mean, 85%) for DDT and from 77% to 106% (mean, 96%) for DDE.

In most instances characteristic Schechter-Haller colors were obtained although in some tests no colors were seen. However, there were a few samples in which colors not characteristic of the Schechter-Haller reaction were found. In samples with atypical colors, small (less than 0.005 mg) quantities of apparent DDT and DDE were involved, and they were not counted as positive.

All of the values for total DDT-derived material (DDT plus DDE) have been expressed in terms of DDT equivalent.

Results

The DDT and DDE contents of the restaurant and household meals analyzed are shown in Table 1.

It is apparent that there was a very large variation in the amounts of DDT and DDE contained in the several meals. There were seven meals (24% of those tested) in the present study which did not contain detectable quantities (less than 0.005 mg) of either DDT or DDE. One additional meal did not contain measurable DDT. No detectable DDE was found in two other meals. In the earlier study DDT and DDE were found in every meal tested.[1]

The one meal which contained the largest amounts of DDT (1.160 mg) and DDE (0.730 mg) represented an amount of each compound somewhat greater than the total of each of these compounds found in all the other meals combined. The single food item which accounted for almost all of this large

TABLE 2.—*Comparison of DDT and DDE Content of Restaurant and Household Meals*

Source	No. of Meals	Total Weight (Including Beverage) (gm)	Total Daily Content (mg) DDT	DDE	Total (as DDT)	DDE (%)
Restaurant	12	2,162	0.038	0.044	0.067	56
Household	17	2,119	0.314	0.173	0.507	38

concentration of DDT and DDE was eggs. This sample represented one to one half poached eggs. Since the eggs were not fried, the high DDT and DDE content could not be ascribed to cooking oil or fat. The eggs were produced locally. The chickens lived in an environment near an agricultural area in which DDT exposure was a distinct possibility, although no specific exposure could be established.

The actual DDT concentration of these eggs was approximately 21 ppm. According to Bryson et al,[4] this level in the egg corresponds to a continued dietary DDT level of about 50 ppm for the hens. This level of DDT intake would be consistent with continued health in the chickens. Bryson and his coworkers noted that chickens withstood up to about 1,250 ppm of DDT in their diet without showing clinical signs of DDT poisoning.

An additional seven samples of eggs were obtained and tested to determine the prevalence of high DDT and DDE content in this foodstuff. One of these samples was obtained from a farmer who kept chickens for the use of his own household. The other egg samples were obtained from six local commercial egg producers. None of these seven egg samples were related to the complete meals under study.

The egg sample from the homegrown chickens showed high DDT and DDE levels similar to those noted above. However, the egg samples collected from the six local commercial egg producers were very much lower

TABLE 3.—*Number of Food Samples Containing Various Amounts of DDT and DDE*

Classification	0.005 Mg or More		0.001 to 0.005 Mg (Trace Quantities)		Less Than 0.001 Mg	
	DDT	DDE	DDT	DDE	DDT	DDE
Beverages	0	0	0	0	10	10
Bread, buttered bread, rolls	1	1	4	5	14	13
Breakfast cereals	0	1	0	0	4	3
Dairy products	1	1	3	2	29	30
Dessert	2	2	1	1	5	5
Eggs, fried	1	2	3	2	1	1
Eggs, poached	1	1	0	0	0	0
Fruits and fruit juices	3	2	1	2	9	9
Hotcakes	1	1	0	1	1	0
Jelly and jam	0	0	0	0	3	3
Macaroni	0	0	0	0	1	1
Meat, gravies, meat combinations	9	4	1	6	11	11
Oleomargarine	2	2	0	0	1	1
Peanut butter	0	0	0	0	1	1
Potato, baked	0	0	1	1	4	4
Potatoes, fried	0	0	0	1	4	3
Potatoes, mashed	0	0	1	1	2	2
Salads	1	0	4	5	7	7
Seafoods	1	1	1	1	2	2
Seasonings	0	0	0	0	2	2
Sirup	0	0	0	0	2	2
Soup	1	1	0	0	0	0
Sugar	0	0	0	0	1	1
Tomato juice	0	0	0	0	1	1
Vegetables	2	2	2	2	14	14
Total	26	21	22	30	129	126

TABLE 4.—*Comparative DDT and DDE Contents of Selected Parallel Food Items Purchased at a "Health Food" Store and at an Ordinary Grocery Store*

Item	DDT Content (Ppm)		DDE Content (Ppm)	
	Health	Ordinary	Health	Ordinary
Fruit, dried				
Apricots	1.20	0.23	0.07	0.06
Figs, brown	0.05	0.04	0.17	0.11
Figs, black	0.05	0.07	0.02	0.17
Peaches	0.41	0.88	<0.02	0.04
Prunes	0.19	0.32	0.04	0.16
Mayonnaise	<0.02	<0.02	<0.02	<0.02
Meat balls	<0.02	<0.02	<0.02	<0.02
Oil, vegetable	<0.02	<0.02	<0.02	<0.02
Salad dressing	<0.02	<0.02	<0.02	<0.02
Stew, beef	<0.02	<0.02	<0.02	<0.02
Mean	0.19	0.15	0.03	0.05

in DDT and DDE content. These samples ranged from <0.02 to 0.20 ppm (mean, 0.11 ppm) for DDT and from <0.02 to 0.17 ppm (mean, 0.10 ppm) for DDE.

Based on all the meals analyzed, the mean daily intake was 0.199 mg of DDT and 0.122 mg of DDE. If the single meal containing the large amount of DDT and DDE was omitted from consideration, then the mean daily intake became 0.086 mg for DDT and 0.061 mg for DDE. The DDE represented 40% of the total DDT-derived material in the complete diet. In the earlier study, DDE constituted 32% of the total DDT-derived material in the diet when the calculation is made in the same way as for the present study.

In Table 2 the comparison for DDT and DDE content between restaurant and household meals is shown. It is interesting to note that the mean total weight of the meal was almost identical for the restaurant meals and for the household meals. However, as noted earlier, the presence of inordinately large amounts of DDT and DDE in one of the household meals increased the mean contents of these chemicals in the household meals to figures much higher than those for the restaurant meals. Even if the single household meal containing the largest amount of DDT is omitted from consideration, the DDT (0.123 mg) and DDE (0.057 mg) content of the household meals is still somewhat higher than that of the restaurant meals (DDT: 0.038 mg; DDE: 0.044 mg). Also, DDE represents a higher fraction of the total DDT-derived material in the restaurant (56%) than in the household meals (38%).

It was considered that the insecticide content of the restaurant meals was more typical of the average DDT and DDE intake for the general population in the United States than was that of the household meals. The restaurant meals represented a more average type of food selection and preparation and did not contain the specialty and home-grown items which many of the household meals in the study contained. Also, it was possible to compare the restaurant meals in the present study with restaurant meals obtained in the earlier study.[1] No household meals were obtained in the 1954 study; therefore, no direct comparison of the 1961-1962 household meals with the earlier study was possible.

Based on the restaurant meals, the present mean daily intake for the general population of the United States is 0.038 mg of DDT and 0.044 mg of DDE. This amount of DDT represents a concentration of about 0.018 ppm in the total wet diet. The DDE represents about 0.020 ppm on the same basis. The total concentration of DDT-derived material in the diet (expressed as DDT equivalent) is about 0.040 ppm. This value represents only about 0.6% of the 7 ppm of DDT allowable as a residue at harvest on certain specified food items and in the meat of some animals destined for human consumption.

In the total dry diet the estimated concentrations were about 0.07 ppm DDT and 0.08 ppm DDE. The concentration of total DDT-derived material was approximately 0.16 ppm.

This DDT intake (0.038 mg) is equivalent to a daily dosage rate for a 70-kg man of about 0.0005 mg/kg.

In Table 3 are shown the numbers of food samples which contained various specified amounts of DDT and DDE. It is noteworthy that in general the products of animal origin (meats, gravies, meat combinations, and eggs) contained the larger quantities of DDT and DDE. Dairy products

TABLE 5.—*DDT and DDE Content of Complete Meals for One Day as Reported by Various Investigators for the Period 1953-64*

Time	Meals: Location	Meals: Source	No.	Total Daily Content, Mg: DDT	DDE	Total (as DDT)	DDE (%)	Reference
1953-1954	Wenatchee, Wash	Restaurant	18	0.178	0.092	0.280	37	
	Tacoma, Wash	Institution (prison)	7	0.116	0.057	0.179	35	1
	Total and Mean		25	0.164	0.083	0.256	36	
1954-1955	Tallahassee, Fla	Institution (prison)	12	0.202	0.050	0.258	21	13
1956-1957	Walla Walla, Wash	Institution (college, meat abstainers)	11	0.041	0.024	0.068	39	12
1959-1960	Anchorage, Alaska	Institution (hospital)	3	0.184	0.028	0.213	14	18
1962-1964	Wenatchee, Wash	Restaurant	12	0.038	0.044	0.087	56	
	Wenatchee, Wash	Household	17	0.314	0.173	0.507	38	This paper
	Total and Mean		29	0.199	0.122	0.335	40	

were an exception to this generality. In the present study a total of 26 food items (15% of those tested) contained quantities of DDT in excess of 0.005 mg, and 21 samples (12%) were of this order of magnitude with regard to DDE contamination. These quantities may be compared with 70 items (42% of the total) for DDT and 42 items (25%) for DDE in the previous study which contained higher than the 0.005 mg level of contamination.

In Table 4 are shown the comparative DDT and DDE contents of selected parallel food items purchased at a "health food" store and at an ordinary grocery store. It is apparent that there was no appreciable difference between the ordinary food items and the so-called "health foods" with regard to DDT and DDE content in this series of tests. It should be noted that, for equal quantities of each item, the cost of the health foods was about twice as great as that of the ordinary items.

Comment

The results reported in this paper are in general agreement with those of other comparable recent studies as shown in Table 5. The total daily intake as reported in the earliest study was estimated to be 0.164 mg for DDT and 0.083 mg for DDE.[1] These figures are about the same order of magnitude as the levels of 0.199 mg for DDT and 0.122 mg for DDE as determined for all meals in the present study. The insecticide levels in each of the intervening (1953-1960) studies listed in Table 5 were also quite similar with the exception of the 1956-1957 study involving meatless meals.[10]

The results reported here are also in general agreement with a somewhat similar study carried out by Mills [5] and Williams [6] of the US Food and Drug Administration. Their work involved determination of the pesticide content of a total diet representing the normal 14-day intake of males 16-19 years old. The daily quantities of food and drink in this diet averaged 3.78 kg. The usual average daily food intake is about 2.20 kg for adults, but adolescent males are known to eat larger quantities of food. The total amount of food was composited, and an aliquot was analyzed. DDT was found in 46 of the 60 total diet samples tested and ranged in concentration from a trace (less than 0.002 ppm) to about 0.020 ppm with a mean of about 0.007 ppm. DDE was de-

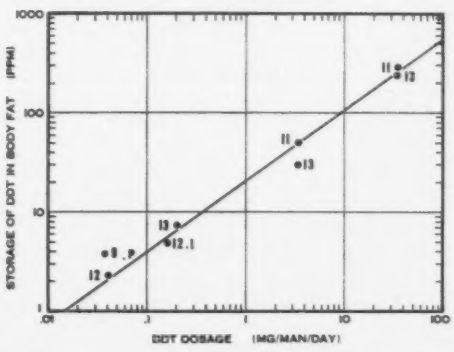

Fig.—Storage of DDT in the body fat of people in relation to dosage. Numbers beside the points refer to references, and "P" indicates this paper.

tected in 30 of the test diets at a mean level of about 0.004 ppm. The calculated daily intake of DDT or other pesticides was not stated. However, a food intake of 3.78 kg and mean dietary concentrations of 0.007 ppm for DDT and 0.004 ppm for DDE would result in daily intakes of about 0.026 mg for DDT and about 0.015 mg for DDE. Similar calculations based on the average adult food intake of 2.20 kg per day give somewhat smaller daily intakes of DDT and DDE. This derived value for daily DDT intake (0.026 mg) is in general agreement with that reported in the present paper (0.038 mg). The daily DDE intake as determined in the two studies (Mills and Williams, 0.015 mg; this paper, 0.044 mg) agree less well but are still within the same order of magnitude.

The amounts of DDT and DDE in restaurant meals were found to be less in 1962-1964 (DDT, 0.038; DDE, 0.044) as compared with 1953-1954 (DDT, 0.178; DDE, 0.092). This apparent decrease in the DDT content of the total diet in the United States between 1953 and 1963 has occurred even though there has been continuing large scale use of DDT. For the period 1950 through 1962, DDT usage in this country has varied appreciably from year to year but has shown no definite trend to increase or decrease although DDT production has increased.[7]

Clifford et al, in comparing the results of their study in 1958 with that in 1955, reported a definite improvement in the situation with regard to pesticide residues in milk.[8] Comparable contamination figures based on the most sensitive method were 67% in 1955 and 33% in 1958. The decrease in DDT in the general diet or in milk alone as found by ourselves and others is not inconsistent with the recent findings of Quinby et al[9] and Hoffman et al[10] who have noted that DDT storage in the general population has remained essentially stable since 1950. It is probable that a decrease in fat storage level would lag behind any diminution of DDT content in the diet since the loss of DDT from storage in fat has been shown to occur slowly.[11]

As shown in the Figure, there is a direct relationship between DDT dosage and DDT storage in man. This figure presents the intake (0.038 mg/day)/storage (3.9 ppm)[9] correlation for the present work and for other studies in which these quantities have been determined. Meat abstainers had a mean daily DDT intake of 0.041 mg and showed an average DDT storage level of 2.3 ppm.[12] The daily dietary DDT intake of 0.164 mg for the general population of this country in 1954 [1] determined a DDT storage level of 4.9 ppm.[12] In a study of prisoner volunteers, the mean daily dietary intake of DDT was found to be 0.202 mg, and the DDT storage level was 7.4 ppm.[13] The higher points on these curves represent values from a study in which volunteers were fed known amounts of DDT (3.5 and 35.0 mg/man/day); and, among other observations, their storage of DDT and DDE and excretion of DDA were measured.[11,13]

Consideration of all factors involved indicates the predominant importance of food as a source of the DDT absorbed by people in the general population. In the present paper the closeness of fit on the DDT intake/storage curve (Figure) of the points whose dosage aspects are determined solely by dietary intake of DDT would seem to indicate that this source accounts for the greater part of the DDT exposure of the general population in this country.

Furthermore, the concentrations of pesticides in potable water are extremely low [14,15] and significant quantities of pesticides have not been reported in air except in work areas. These facts confirm the conclusion reached independently by Campbell that food contributes over 90% of the DDT absorbed by people in the general population.[16]

Further studies are needed to determine the daily dietary intake for other pesticides including BHC and dieldrin which have recently been detected in the United States in the general diet [5,6] and in the fat of the general population.[17]

Summary

The DDT and DDE contents of 29 complete prepared meals were determined. Seven meals contained no detectable DDT or DDE. One additional meal did not contain meas-

urable DDT. No DDE was found in two other meals.

The one meal which contained the largest amounts of DDT (1.160 mg) and DDE (0.730 mg) represented an amount of each compound somewhat greater than the total of each of these compounds found in all the other meals combined. The single food item which accounted for almost all of this large concentration of DDT and DDE was one to one and a half poached eggs. Since the eggs were not fried, the high DDT and DDE content could not be ascribed to cooking oil or fat.

Based on all the meals analyzed, the mean daily intake was 0.199 mg of DDT and 0.122 mg of DDE. If the single meal containing the large amounts of DDT and DDE were omitted from consideration, then the mean daily intake became 0.123 mg for DDT and 0.057 mg for DDE.

The household meals in this study contained somewhat higher concentrations of DDT and DDE than did the restaurant meals. Since they represented a more average type of food selection and did not contain specialty or homegrown items, the restaurant meals were considered to be more typical of the average American diet than were the household meals. Based on the restaurant meals, the present mean daily intake for the general population of the United States is 0.038 mg of DDT and 0.044 mg of DDE. This amount of DDT represents a mean concentration of about 0.018 ppm in the total wet diet. This DDT intake is equivalent to a daily dosage rate for a 70-kg man of about 0.0005 mg/kg.

Comparison of the results of the present study with those of earlier studies indicates that the DDT content of the total diet has decreased between 1953 and 1963.

In general the products of animal origin (meats, gravies, meat combinations, and eggs) contained the larger quantities of DDT and DDE. Dairy products were an exception to this generality.

There was no appreciable difference between food items purchased at an ordinary grocery store and similar items purchased at a "health food" store with regard to DDT or DDE content.

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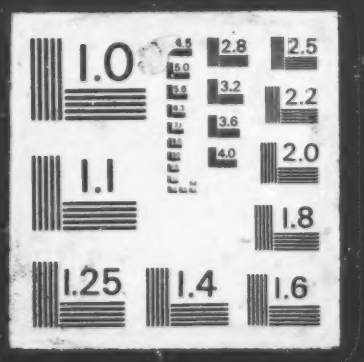

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Dichlorodiphenyltrichloroethane and Dichlorodiphenyldichloroethylene Content of Prepared Meals

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Small quantities of DDT and DDE have been found in the body fat of humans. DDT has had wide use on food and forage crops and for control of insect-borne diseases. DDT and DDE were found in all meals analyzed, but in small quantities, and are not considered a toxicological health hazard. In the case of foods intended for human consumption, the DDE content as well as the DDT content should be determined.

THE FINDING of small quantities of dichlorodiphenyltrichloroethane (DDT) and dichlorodiphenyldichloroethylene (DDE) in the body fat of humans (*16, 18*) with no known direct exposure to DDT or DDE raises the question of the quantity of these compounds ingested with normal food intake.

The use of DDT for the control of insects affecting man and animals is well established and the compound has been applied to almost all food and forage crops. Though not currently recommended, DDT has been applied to dairy cattle and dairy barns for fly control and its secretion in butterfat has been established (*15*), as it has in dairy cattle fed vine silage or alfalfa hay containing DDT (*4, 19*). Foodstuffs have been contaminated by the impregnation of sacking (*2*) and DDT has been added to drinking water for the control of mosquitoes (*12*). DDT spray residues have been reported on fruits (*3*), on bread and cake made from DDT-treated flours (*11*), and on milled products (*10*).

The results of experimental feeding of DDT to dogs, its accumulation in the body fat, and its appearance in the milk of dogs have been reported (*22*). The storage of DDT in the tissue of pigs (*5*) and sheep (*13*) and its transfer from feed to eggs and body tissue of chickens (*6*) under experimental conditions have also been reported.

The storage of DDT in human fat was reported in 1948 (*14*) and in human milk in 1951 (*9*). Pearce, Mattson, and Hayes (*18*) pointed out that much of the reported DDT in human fat was actually the degradation product, DDE.

Methods

Collection Of Meals To determine the amounts of DDT and DDE ingested during normal food intake, 18 meals were obtained from restaurants and 7 were obtained from a correctional institution. Most of the food prepared by the restaurants was not locally grown. Much of the food consumed at the correctional institution was produced within the institution itself. Regional items, such as fresh sea food and unusual foods, were avoided, so that a representative cross section of food items consumed by the public could be obtained. Home-cooked meals also were avoided because of the difficulty of obtaining a representative cross section.

The individual items comprising the meals were collected in chemically clean glassware directly from the kitchen of the restaurant or the institution, in order to obtain the samples in containers known to be free of DDT and to prevent the contamination of one food with another. In some instances the portions obtained were much larger than those usually served. Where such discrepancies were noted, the samples were reduced to reasonable portions before proceeding with the analysis. Upon receipt of the samples at the laboratory, each item was weighed after the inedible portions had been removed.

Extraction And Analysis The edible portions were extracted with acetone in a blender and filtered, and the filter cake was extracted with carbon tetrachloride in a large Soxhlet extractor. The two extracts were concentrated and combined for analysis. Prior to the final analysis, the combined extracts were chromatographed by a modification of the method of Davidow (*21*) for the removal of interfering fats and plant pigments. In certain individual portions the fat content was fairly high. Because it is not practical to remove more than 2 or 3 grams of fatty material with the modified Davidow column, an aliquot of the samples was chromatographed. If the amount of DDT and/or DDE in this aliquot was less than the lower limit of sensitivity of the method, such samples were reported on the basis of the aliquot taken and not on the basis of the entire sample; the entire samples may have contained determinable amounts of DDT or DDE. DDT and DDE were determined by a modified Schechter-Haller procedure (*16, 21*).

Prior to analysis, several of the food items were divided into equal parts. One half of each sample was analyzed in the regular manner; the other half was analyzed after addition of known amounts of DDT and DDE. The recovery of known amounts of DDT averaged 73.7% with a range of recoveries from 40.0% for French toast to 110.0% melted butter. The recovery of known amounts of DDE averaged 82.2% with a range of from 66.1% for toast to 103.0% for melted butter.

Brittin and Faring (*1*) were able to recover 51.2% of the DDT they added to strained peaches, pears, peas, green beans, and vegetable and beef soups. Tressler (*20*) recovered 89% of the DDT added to strained peaches and 61% of the DDT added to applesauce. The formation of emulsions with organic solvents used in the extraction procedure and the difficulty of breaking these emulsions in order to obtain complete recovery of the DDT-bearing organic solvent layer probably account for most of the added DDT lost.

The analytical method employed enables estimation of 5 γ of either DDT or DDE with an accuracy of approximately 10%. Values below 5 γ for either compound may be subject to considerable error due to the effect of interfering colors from the sample. For this reason values below 5 γ can be considered only an approximation. One microgram of DDT and/or DDE can be detected in control samples where no interfering colors are present. In totaling the individual food items of the 25 meals, the value of 2.5 γ was used for food items that contained between 1 and 5 γ of DDT or DDE.

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The results obtained on the individual portions were combined into the original meals, including eight morning, nine noon, and nine evening meals. Table I presents a summary of the analyses of these meals.

Results

As will be noted, portions of nine meals were lost during analysis. Analysis of subsequent samples indicated that the loss of samples of fried eggs from meal 3, and of cherry pie a la mode and sliced lemon from meal 18, may have affected the total DDT and/or DDE content of these two meals. The loss of items from the other meals probably did not reduce the total DDT and/or DDE content of these meals by more than 5 γ per item. The effect of the loss of a sample of grapefruit from meal 16-IM could not be determined, as only one sample of grapefruit was obtained in all the meals analyzed.

One of the significant results of these analyses is the finding of relatively large portions of DDE in the meals. In individual meals the ratio of DDE to DDT ranged from 0.21 to 1 up to 1.55 to 1 with an average of 0.50 to 1. Three noon meals contained more DDE than DDT, but in each case a large amount of the DDE was confined to a few food items. The finding of DDE in food emphasizes the importance of separating DDE from DDT in studies of residues on food products ultimately intended for human consumption; not only does the DDE represent less potential health hazard while stored in the body fat, but a portion of the DDE found in the fat may have never existed as the more toxic DDT in the human body.

Every meal analyzed contained both DDT and DDE. Institutional meals in general contained about the same amounts of DDT and DDE as did restaurant meals, except in the cases of the morning meals. The institutional breakfasts consisted only of cereal, milk, fruit, breakfast rolls, and margarine and contained none of the fried foods which account for most of the DDT and DDE in restaurant meals.

Aside from this, the amount of DDT in the three types of meals was roughly proportional to the size of the meal. The noon and evening meals contained about the same amount of DDE regardless of size.

A total of 179 individual portions of food representing 86 different items was included in the 25 meals, and of these 40 contained insufficient DDT to be detected. Ten other samples showed no DDT, but these 10 samples had been so reduced in size in order to reduce the fat content that they cannot be included with assurance in the DDT-free group.

The individual portions of the 25 meals were divided into 21 classifications. The number of samples within a classification that contained 5 γ or more, 1 to 5 γ, and less than 1 γ of DDT and DDE are listed in Table II.

Generally those foodstuffs cooked in fat, and containing meat, meat combinations, or butter, were found to have a higher DDT content than foodstuffs not cooked with fat, and not containing meat, meat combinations, or butter. DDE content was roughly porportional to the DDT content. A few individual food classifications are worthy of note.

Discussion

Beverages. The three samples that contained trace quantities of DDT and the two samples that contained trace quantities of DDE were coffee with added cream. All other beverages contained no cream.

Potatoes, Mashed. The two samples that contained trace quantities of DDT and DDE also contained added butter. The other six DDT-free samples contained no added butter.

Breakfast Cereals. The one sample that contained a measurable quantity of DDT was cooked oatmeal. An additional sample of cooked oatmeal did not contain a measurable quantity of DDT.

Fruit and Fruit Juices. One sample of pitted prunes (dried fruit that had been cooked) contained a measurable quantity of DDT.

Vegetables. Of the 21 samples of vegetables (peas, beans, corn, lima beans, tomatoes, mixed vegetables, swiss chard, beets, carrots, cabbage, and soups), 8 samples contained 5 γ or more of DDT and 1 sample contained 5 γ or more of DDE. Two of the 8 samples, lima beans and carrots, contained 15 and 21 γ, respectively, of DDT. The lima beans had been cooked with ham and the carrots were prepared in a white cream sauce. The creamed carrots contained DDT and DDE, while the lima beans contained DDT only.

Sea Foods. The sea foods contained a greater quantity of DDE than DDT. Two of the three samples (oysters and halibut) had been fried in deep fat; the other sample was clam chowder. No DDT but an appreciable quantity of DDE was found in the chowder.

Bread, Buttered Bread, and Sweet Rolls. More DDT was found on the buttered bread and sweet rolls (having a

Table I. DDT and DDE Found in Typical Restaurant and Institutional Meals

Meal	Total Weight (Including Beverage), Grams	Total Found, γ		Ratio of DDE/DDT
		DDT[a]	DDE[b]	
Morning				
1	527	27.5	12.5	0.46
2	443	62.5	30.5	0.49
3	522[c]	59.5	24.5	0.41
4	728[d]	48.0	26.5	0.55
5	536[e]	70.0	47.5	0.68
6	731	27.5	8.5	0.31
7-IM	805	8.5	5.0	0.59
8-IM	383[f]	10.0	5.0	0.50
Mean	584	39.2	20.0	0.51
Noon				
9	701[g]	40.0	23.5	0.59
10	848	163.5	44.5	0.27
11	687	16.5	21.0	1.27
12	987	17.0	17.5	1.03
13	805	65.5	50.0	0.76
14	689	37.5	58.0	1.55
15-IM	1508	34.5	15.0	0.44
16-IM	652[h]	79.0	25.5	0.32
17-IM	548	71.5	30.0	0.42
Mean	825	58.3	31.7	0.54
Evening				
18	666[i]	118.0	43.0	0.36
19	900	46.0	40.5	0.88
20	1017[j]	161.5	34.5	0.21
21	1196	51.0	31.5	0.62
22	1108	32.5	27.0	0.83
23	914	34.0	12.5	0.37
24-IM	1083[k]	50.0	30.5	0.61
25-IM	1288	39.5	27.0	0.68
Mean	1022	66.6	30.8	0.46
Mean of all meals	811	54.8	27.7	0.50

IM Institutional meals.
[a] Calculated as technical DDT.
[b] Calculated as recrystallized DDE.
Amounts lost on analysis and not included in totals. [c] 140 grams. [d] 49 grams. [e] 42 grams. [f] 192 grams. [g] 471 grams. [h] 75 grams. [i] 193 grams. [j] 268 grams. [k] 51 grams.

frosting or a jelly filling) than on the unbuttered bread.

Dairy Products. Though the correctional institution reported that margarine was used, all the restaurants reported their spreads as butter. Whether or not they actually were butter was not determined, but they are included with dairy products in Table II. Because of considerable doubt as to the validity of this assumption, butter was not included in Table III. Six of these samples contained measurable amounts of DDT, four contained between 1 and 5 γ, and four contained less than 1 γ. Seven servings of oleomargarine were obtained from the correctional institution, but as they were all from the same lot, only one sample was analyzed and reported separately in Table II. It contained less than 1 γ of DDT. A milkshake contained more DDE than DDT.

Seasonings. One sample of mayonnaise and one sample of barbecue sauce contained measurable quantities of DDT and DDE. The barbecue sauce contained a little more than twice as much DDT as DDE.

Bread, Fried. The term "bread, fried" was used to cover hot cakes, pancakes, and French toast. Three samples contained measurable amounts of DDT and two out of the three contained measurable amounts of DDE.

Desserts. Three out of four samples of pie contained DDT and two of these samples contained DDE. One sample of mince pie contained more DDT than any other food item except meat.

Potato, Baked. The one sample of baked potato had a very glossy appearance, indicating that it had been brushed with melted butter. The DDT and DDE content of the baked potato (entire potato including the skin) confirmed this observation.

Meats, Gravies, and Meat Combinations. Twenty-four of the 27 samples of meats, gravies, and meat combinations (meat loaf, chile con carne, spaghetti and meat balls) had measurable quantities of DDT. Twenty out of the 27 contained measurable quantities of DDE. In one sample of boiled beef tongue there was approximately four times as much DDE as DDT. Several of the samples (such as gravies) were reduced in size, owing to their fat content, and the aliquot taken for analysis did not contain measurable quantities of DDT and/or DDE.

Potatoes, Fried. All seven samples of fried potatoes, (fried, French-fried, and hashed-brown) contained measurable quantities of DDT. Three of the seven samples contained determinable amounts of DDE.

Eliminating duplication, 28 foods are listed in Table III, one or more portions of which did not contain detectable (1 γ) amounts of DDT. Some of these foods, however, were represented by other portions which did contain measurable (5 γ or more) quantities of DDT. Most o the remaining foods listed in the table represent foods that were analyzed only once.

To date there is no precise information as to the amount of DDT which can be consumed by humans over a long period of time without the possibility of adverse results. Basing his conclusion mainly on chronic toxicity studies conducted on laboratory animals, but taking a safety factor into account, Neal (*17*) estimated that 5 mg. of DDT can be ingested daily without untoward effects. Fitzhugh (*7*) and Heyroth (*8*) estimated that man can ingest 2.5 mg. of DDT daily over a long period of time without injury.

If an individual were to consume in one day the three meals found to contain the highest amounts of DDT (meals 2, 10, and 20), his total DDT intake would be 0.388 mg. or 15.5% of the smaller amount which it has been estimated that humans could consume regularly without adverse effects. The average daily intake based on all meals would be about 0.184 mg. of DDT per day. This is equivalent to a dosage of about 0.0026 mg. per kg. per day for a man of average size or a concentration of about 0.31 p.p.m. of DDT in the total dry diet. By comparison, a rat would have to eat a diet containing about 0.05 p.p.m. to obtain the same dosage, because the rat eats more food than man in proportion to body weight.

Table II. Number of Samples Containing DDT and DDE

Classification	5 γ or More		1 to 5 γ (Trace Quantities)		Less than 1 γ	
	DDT	DDE	DDT	DDE	DDT	DDE
Oleomargarine	0	0	0	0	1	1
Beverages	0	0	3	2	14	15
Potatoes, mashed	0	0	2	2	6	6
Breakfast cereals	1	0	2	4	3	2
Sirup	0	0	2	1	1	2
Salads	0	0	2	1	1	2
Potatoes, escalloped	0	0	1	1	1	1
Fruits and fruit juices	1	0	5	4	2	4
Macaroni	0	0	1	1	0	0
Vegetables	8	1	7	11	6	9
Seafoods	1	3	1	0	2	1
Bread, buttered bread, and sweet rolls	6	2	7	10	3	4
Dairy products	7	3	4	3	4	9
Seasonings	2	2	1	1	2	2
Bread, fried	3	2	0	1	0	0
Dressing, bread	1	0	0	1	0	0
Dessert	6	3	5	7	1	2
Potato, baked	1	1	0	0	0	0
Meat, gravies, and meat combinations	24	20	2	5	3	4
Potatoes, fried	7	3	0	2	0	2
Eggs, fried	2	2	0	0	0	0

Summary and Conclusions

DDT was present in detectable but very small quantities in all meals analyzed.

DDE was present in all meals, though in somewhat lower quantities.

Few if any foods can be relied upon to be entirely free of DDT.

Fried foods, and those having a high fat content, either natural or added, contained more DDT than other types of foods.

In general, high DDE content of foods is associated with high DDT content, though it is possible to have measurable DDE in the absence of DDT and measurable DDT in the absence of DDE.

No meals contained enough DDT to be considered a toxicological health hazard on the basis of the estimated chronic oral toxicity of the compound.

DDT residues on foods ultimately intended for human consumption should be assayed in such a way that the DDE content as well as the DDT content would be determined.

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Table III. Foods Without Detectable (1 γ) Amounts of DDT

Applesauce	Corn[a]	Potatoes, mashed[a]
Beans, string[a]	Corn bread	Rolls[a]
Bean soup	Dry cereal[a]	Root beer
Cake[a]	Grapefruit juice	Steak, pan broiled[b]
Catsup	Gravy[a]	Sirup[a]
Clam chowder	Jello salad	Tea[a]
Coffee, black	Oleomargarine	Toast[a]
Cola beverage	Peas[a]	Tuna fish salad
Combination salad	Potatoes, escalloped[a]	Vegetables, mixed
		Vinegar

[a] Other portions contained a measurable amount of DDT (5 γ or more).
[b] Calculation based on aliquot chromatographed.

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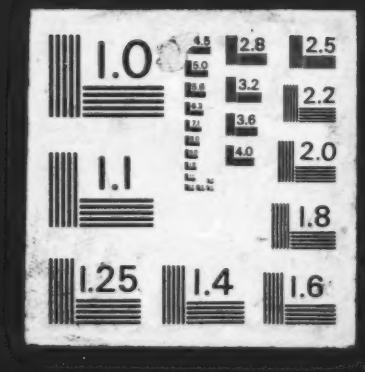

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PESTICIDES PROGRAM
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MONITORING FOOD AND PEOPLE FOR PESTICIDE CONTENT

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Monitoring Food and People for Pesticide Content

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The purpose of this paper is to outline what is already known about the scientific principles of absorption, storage, and excretion and about the occurrence of pesticides in our food and in our bodies; how studies of these things are being expanded; and why our concepts need to be carefully evaluated.

The Relation of Absorption, Storage, and Excretion

Before discussing the measurement of pesticides in food and people, I shall present a few general principles. All compounds that are absorbed by the body may be said to be stored as long as they remain in the body. The degree of storage and its duration vary greatly, depending primarily on the compound and secondarily on its dosage. Other factors that influence storage include species, sex, and age.

In general, compounds that are water soluble can be excreted easily by the body, although they may undergo some chemical change before they are eliminated entirely. Compounds that are

not water soluble must be made soluble before they can be excreted. This solubilization may be accomplished through chemical breakdown of the compound or through its conjugation with some naturally occurring material in the body to form a soluble complex. All such changes of foreign compounds in the body are spoken of as their metabolism. Some compounds are metabolized much more slowly than others and therefore are retained in the body longer and accumulate to a greater degree at any given dosage rate.

Although foreign compounds may be metabolized in many tissues of the body, the organ particularly adapted to this function is the liver. Materials that, because of solubility and other properties, reach a relatively high concentration in the liver are thus available for the most efficient metabolism of which they are capable. On the other hand, compounds like DDT (dichlorodiphenyltrichloroethane), which reach their highest concentrations in fat, or materials like lead, which reach their highest concentrations in bone, are, by the same token, poorly available to the liver and its metabolizing action. Thus, materials differ in their storage because of differences in their need for metabolism, their ease of metabolism, and their availability for metabolism.

It has been observed that nearly all drugs are excreted from the body in such a way that a constant proportion of the amount present in the body is lost per unit time. Studies of the rate of storage loss for phenobarbital,[12, 67] barbital and aprobarbital,[67] pamaquine,[113] caffeine,[5] creatinine,[27] theophylline,[102] sulfathiazole and sulfapyridine,[42] penicillin,[41, 91] tetracycline,[73] and streptomycin [9] have illustrated this principle.

For a rapidly excreted drug such as aspirin this proportion in man is approximately 47 percent per day.[37] For a more slowly excreted drug such as phenobarbital the proportion in man is 14 to 27 percent per day.[67]

The general principle of the relationship between absorption, storage, and excretion may be illustrated by a comparison to banking in which deposit is analogous to a fully absorbed dose and withdrawal is analogous to excretion. If one deposits exactly $1.00 on each banking day and also on each of these days withdraws half of the balance (leaving any fraction of a cent in the bank in order to increase the balance or storage), then the amount remaining in the bank each morning before the processes of deposit and withdrawal are carried out would increase rapidly at first then more slowly until a steady state is reached. The actual values for the second and succeeding days are $0.50, $0.75, $0.88, $0.94, $0.97,

$0.99, and $1.00. From then on, according to our very simple model, the deposit each day will be $1.00, the withdrawal will be exactly equal to it, and $1.00 will remain in the bank each morning to represent net storage.

Not all compounds follow the simple rule by which a constant proportion of the stored material is lost per unit time. Some compounds, such as radium, interfere with their own excretion either through progressive sequestration in bone or, as postulated by Norris and Kisieleski,[82] through direct injury to the mechanism necessary for excretion. A decreasing proportion of such materials is excreted as time goes on.[83] Other compounds behave in exactly the opposite way, perhaps because a sufficient concentration of them in the body stimulates their own metabolism. In any event, we have found that the loss of DDT from storage, although always slow (less than 0.3 percent per day in man), is always more rapid when the storage is high than when it is low. Thus, the rate of excretion of DDT changes with concentration while that of the bone-seekers changes with time.

The important principle is that all compounds reach or at least approach a steady state of storage, provided the dosage is constant and is tolerated by the organism. It is important to know that for a given compound and species there will be a different level of storage for each dosage. In general, doubling the dosage will double the storage, but in some instances storage may not increase quite as rapidly as dosage.

What the storage corresponding to a given dosage will be and how long it will take to reach a steady state can be estimated if one is familiar with the behavior of other compounds of the same chemical group. However, in order to be exact, the equilibrium value and the time necessary to achieve it must be determined by observation for each individual compound.

It follows from what has been said that our bodies contain at least a trace of all of the materials we absorb. Thus, the storage of lead, mercury, and arsenic [77] is universal, because they are elements that are widely distributed in nature and that occur in a wide range of foods, including many never treated with pesticides of any kind.

Lead is a good example of a cumulative poison. Although lead compounds may undergo chemical reaction, their toxicity is never lost, because it is inherent in the lead atom. Lead in any form is poorly excreted; and, therefore, the degree of storage tends to be high in relation to dosage.

In contrast with lead and other heavy metals, the modern synthetic pesticides are capable of detoxification. In fact, most of them are metabolized efficiently and excreted rapidly so that they can be measured only in the tissues or excreta of people with significant exposure and then only for a brief time after exposure. For example, men who were dusted all over with malathion excreted up to 9.57 mg per hr in their urine, but excretion decreased precipitously after the last application and was indistinguishable from control values by the third day after the last application.[52] In fact, these same compounds are subject to spontaneous breakdown under the influence of moisture, sunlight, and other environmental factors. They are also subject to action by the enzymes of plants. Thus, as the result of chemical and enzymatic change, residues of these compounds tend to be destroyed so that they may be no longer present when the crop to which they were applied is harvested.

The main exception among the newer compounds is the chlorinated hydrocarbon insecticides. These materials are not as stable as the heavy metals. They are broken down both chemically and enzymatically both on crops [74] and in the soil,[65, 66] but the rate of these changes is slow with the result that traces of the compounds occur in our food and are absorbed by our bodies. Their metabolism in mammals has been reviewed elsewhere.[48]

Monitoring Pesticides in Food

A review [45] shows that the occurrence of DDT residues on crops to which the insecticide was applied was recognized and measured at least as early as 1945.[44] Apparently, the earliest effort to learn how much DDT the average man obtains from his daily food was that of Walker and his colleagues,[108] summarized together with later surveys and special studies in Table 1. In 1953 and 1954, Walker and his colleagues analyzed the individual items constituting typical restaurant meals. DDT was found in every meal but not in every kind of food. The greater proportion was in meat and other food of animal origin. The average amount in the three meals a person would eat each day was 0.178 mg.

Monitoring of milk was carried out on several occasions by the U.S. Food and Drug Administration (FDA).[14, 15] Although traces of DDT were found, the proportion of samples that were positive and the concentration of DDT in these samples gradually decreased over a period of years. Later, the famous series of "Market Basket"

Table 1.
Estimated Daily Content of DDT and DDE in Complete Meals in the United States

Year	Location	Source	Number	Total Daily Content, mg: DDT	DDE as DDT	Total as DDT	DDE as DDT (% of total)	Reference
1953–1954	Wenatchee, Wash.	Restaurant	18	0.178	0.102	0.280	37	(103)
	Tacoma, Wash.	Prison	7	0.116	0.063	0.179	35	
1954–1955	Tallahassee, Fla.	Prison	12	0.202	0.056	0.258	21	(50)
1956–1957	Walla Walla, Wash.	College dining room for meat abstainers	11	0.041	0.027	0.068	39	(51)
1959–1960	Anchorage, Alaska	Hospital	3	0.184	0.029	0.213	14	(29)
1961–1962	Washington, D.C. Baltimore, Md. Atlanta, Ga. Minneapolis, Minn. San Francisco, Calif.	Market Basket survey	36[a]	0.026[b]	0.017[b]	0.043[b]	40[b]	(76)
1962–1964	Wenatchee, Wash.	Restaurant	12	0.038	0.049	0.087	56	(32)
	Wenatchee, Wash.	Household	17	0.314	0.193	0.507	40	
1962–1964	Atlanta, Ga. Baltimore, Md. Minneapolis, Minn. St. Louis, Mo. San Francisco, Calif.	Market Basket survey	23[a]	0.023[b]	0.013[b]	0.036[b]	36[b]	(109)
1964	Baltimore, Md.	Market Basket survey	1[a]	0.023[b]	0.017[b]	0.040[b]	43[b]	(18)

[a] This figure refers to the number of diet samples, each consisting of the total normal 14-day food intake for males 16 to 19 years old, which were tested. In some instances, additional diet samples were taken and aliquots were analyzed for pesticide content of various classes of foodstuffs, but no composite value was given.

[b] The author did not calculate the daily DDT or DDE intake. However, using the author's mean dietary concentrations of DDT and DDE and the mean daily food intake of 3.78 kg from the Market Basket survey, the reviewer has calculated the values shown.

studies was carried out by the FDA.[18, 28, 78, 109] A wide range of foods sufficient to feed a 16- to 19-year-old boy for a week was purchased from ordinary grocery stores in cities in different parts of the country. This particular plan was selected because it is known that 16- to 19-year-old boys eat more than any other individuals in our population. The results again showed traces of DDT in some, but not in all, total-diet samples. Although the authors failed to calculate the rate of intake of DDT, which would be determined by the Market Basket samples, this rate has been calculated from data they supplied,[32] and it is 0.026 mg per man per day. Although the daily intake for Canada has not been calculated, both the frequency and the concentration of pesticides in whole meals there apparently is even lower than in this country.[100]

If one considers the inherent difficulty of the chemical method for such small traces, the results of the Market Basket samples are in good agreement with those found in a second study of complete restaurant meals. In repeating the earlier work of Walker *et al.*,[103] Durham *et al.*[32] found that a person who ate regularly in the restaurants sampled would receive an average of 0.038 mg per man per day. This represented less than one fourth of the average rate of DDT intake measured 11 years earlier in the same laboratory.

The most important monitoring of our food in regard to pesticides is that carried out each year by the FDA in connection with food shipped in interstate commerce and by comparable agencies in different states in regard to food brought to market within their own jurisdictions. The samples are taken for the purpose of enforcing the Food, Drug, and Cosmetic Act of 1938, as amended, and corresponding state laws, and not for the purpose of learning the average pesticide intake. The federal government alone now analyzes over 26,000 samples per year, which constitutes approximately 1 percent of the total food shipped in interstate commerce.[78] Among the states, California apparently carries out the most extensive program of testing food products for pesticide residues. During 1964, the California State Department of Agriculture tested 14,596 samples of foods and feeds for pesticide residues.[95] Of these, 537 samples (3.7 percent) were found to contain residues in excess of the tolerance level. The biggest problem associated with illegal residues was encountered not with food intended directly for man, but with hay and fodder crops. Of 3,253 samples of these commodities analyzed, 405 samples (12.5 percent) contained residues in excess of the low tolerance level set for them.

Many of the samples, both federal and state, are taken from shipments suspected of containing excessive residues. Suspicion is based on information regarding use of pesticides, which tends to be heavier in certain places and in certain seasons where conditions are particularly favorable for crop pests.

This kind of monitoring tends to give information on maximal potential intake of pesticides rather than on typical intake. Enforcement of the law, which is an integral part of the monitoring, is a powerful force to prevent illegal residues of pesticides from reaching the consumer market.

The surveys of milk, the Market Basket surveys, and the selective sampling of slightly over 1 percent of our entire food supply concerns not only DDT but all of the chlorinated hydrocarbon insecticides and a wide range of other compounds as well. In general, DDT has been found at higher average concentrations than any of the other chlorinated hydrocarbon insecticides. Of course, analyses carried out for the purpose of enforcement occasionally reveal exceptions. An example may be found in the seizures of large shipments of potatoes and carrots in the Pacific Northwest in 1962 because they contained excessive residues of aldrin and dieldrin.[78] Aldrin had been applied not to the vegetables but to the soil in which they were grown. Corrective measures were taken, and excessive residues were not found during the following year.[78]

Water is really a part of our food. A substantial proportion of the measurements of pesticides in water have involved streams or ponds to which pesticides were added intentionally; most others concerned water suspected of being contaminated, for example, by runoff from fields where crops had been treated by economic poisons. Such analyses would tend to indicate a higher concentration of pesticides than would be expected in the average drinking water. Although pesticides have been found in raw [10, 80, 96, 105] and finished [80] drinking water, and even in rainwater,[108] the concentrations were usually extremely small. Apparently, the highest concentration (0.02 ppm) was that reported quite early for DDT in certain rivers and lakes.[78] The highest concentration reported for any insecticide in the most recent and most comprehensive survey was 0.00012 ppm for dieldrin,[105] and many of the samples contain no detectable pesticide. Six insecticides or metabolites—dieldrin, endrin, DDT, DDE (dichlorodiphenyldichloroethylene), DDD (tetrachlorodiphenylethane), and aldrin—were found in measurable amounts in some samples, and heptachlor and BHC (benzene

hexachloride) were presumptively present in a few samples. The average concentration for the six compounds combined was 0.000023 ppm for the entire survey.[103] Based on this concentration and the usual assumption that each person drinks 2 liters of water each day, it may be calculated that the intake of chlorinated hydrocarbon insecticides from water would be 0.000046 mg per person. Even an estimate based on the highest concentration of any pesticide in water reported in recent years, i.e., 0.001 ppm for BHC,[89] would be only 0.002 mg per person.

Monitoring Pesticides in People

The storage of DDT in one man was first reported in 1948 [57] and was undoubtedly present in the general population even earlier. However, samples taken from people before DDT was manufactured did not contain the compound or anything else giving a similar reaction on analysis [51] (Table 2). The first general survey for DDT was carried out by Laug and his colleagues in Washington, D.C., in 1950 and was reported in 1951.[63] More recent studies in the United States have been made by Hayes *et al.*,[50, 51, 54] Dale and Quinby,[20] Hoffman *et al.*,[53] Quinby *et al.*,[88] and Zavon *et al.*[112] Similar studies have been made in Canada,[92] England,[34, 58, 94] Germany, [69, 70] Hungary,[25] France,[53] Israel,[104] and India.[28] The results show that DDT is found in virtually everyone in the general population of this and other countries (Tables 2 and 3). There has been no increase in the storage of DDT by the general population of the United States since it was first measured in 1950.[51, 56, 88] Studies in volunteers have shown that the excretion of DDT is very slow in man.[58] As pointed out by Durham *et al.*,[32] it is probably too early to recognize any decrease in storage of DDT in the general population that may be occurring as the result of the decrease of DDT in our food mentioned previously.

The storage of DDT in people with special environmental, occupational, or other special exposure to the insecticide is summarized in Table 4. Meat abstainers [51] and Eskimos,[29] whose diet is relatively free of DDT, store significantly less of it than most people do. On the other hand, people with occupational exposure to the compound store more of it.[51] Apparently, the highest recorded storage in a healthy man was 648 ppm measured in the fat of a formulator.[50] This value is 162 or more times the average storage found in the general population in separate investigations since 1960 (Table 2).

Table 2.
Concentration of DDT-Derived Material in Body Fat of the General Population of the United States

Year	Location	No. of Samples	Analysis Method	DDT (ppm)	DDE as DDT (ppm)	Total as DDT (ppm)	DDE as DDT (% of total)	Reference
<1942	Louisville, Ky.	10	Colorimetric	[a]	[a]	[a]	—	(51)
1950	Washington, D.C.	75	Colorimetric	5.3	—	5.3	—	(63)
1955	Tallahassee, Fla.	49	Colorimetric	7.4	12.5	19.9	63	(50)
1954–1956	Savannah, Ga. and Wenatchee, Wash.	61	Colorimetric	4.9	6.8	11.7	58	(51)
1956	Atlanta, Ga.	36	Colorimetric	5.5	10.1	15.6	65	(55)
1961–1962	Atlanta, Ga., Louisville, Ky., Phoenix, Ariz., and Wenatchee, Wash.	130	Colorimetric	4.0	8.7	12.7	69	(88)
1961–1962	Wenatchee, Wash.	28[b]	GLC[c]	2.4	4.3	6.7	64	(20)
1962–1963	Chicago, Ill.	282	GLC[c]	2.9	8.2	11.1	74	(56)
1964	Northeast, Midwest, Deep South, and Far West	64	GLC[c]	2.5	5.1	7.6	67	(112)
1964	New Orleans, La.	25	GLC[c]	2.3	8.0	10.3	77	(54)

[a] Not detected.
[b] These 28 samples were also tested for DDT and DDE content by a colorimetric method (see Table 5). These results are included in the 130 samples listed above.
[c] Gas-liquid chromatography.

Table 3.
Concentration of DDT-Derived Material in Body Fat of the General Population of Countries Other Than the United States

Country	Year	No. of Samples	Analysis Method	DDT (ppm)	DDE as DDT (ppm)	Total as DDT (ppm)	DDE as DDT (% of total)	Reference
Canada	1959–1960	62	Colorimetric	1.6	3.3	4.9	67	(92)
Germany	1958–1959	60	Colorimetric	1.0	1.3	2.3	57	(70)
England	1961–1962	131	Colorimetric	—	—	2.2	—	(58)
England	1963–1964	66	GLC*	1.1	2.2	3.3	67	(34)
England	1964	100	GLC*	—	—	3.9	—	(94)
France	1961	10	Colorimetric	1.7	3.5	5.2	67	(53)
Hungary	1960	48	Colorimetric	5.7	6.0	12.4	48	(25)
India (Delhi area, civilian)	1964	67	Colorimetric	16	10	26	39	(23)
India (other cities, military)	1964	16	Colorimetric	8	5	13	37	(23)
Israel	1963–1964	254	Colorimetric	8.5	10.7	19.2	56	(104)

* Gas-liquid chromatography.

Table 4.

Concentration of DDT-Derived Material in Body Fat of People in the United States with Special Exposure (Environmental, Occupational, or Dietary) to DDT [a]

Exposure	Year	No. of Samples	DDT (ppm)	DDE as DDT (ppm)	Total as DDT (ppm)	DDE as DDT (% of total)	Reference
Died before DDT	<1942	10	[b]	[b]	[b]	—	(51)
Environmental [c]	1954–1956	110	6.0	9.6	15.6	62	(51)
Environmental [c]	1961–1962	28	4.3	8.6	12.9	67	(88)
Applicators	1954–1956	30	14.0	21.1	35.1	60	(51)
Applicators	1961–1962	14	10.7	24.1	34.8	69	(88)
Formulator	1951	1	122	141	263	54	(72)
Formulator	1954	1	648	483	1131	43	(50)
Meat abstainers	1955–1956	16	2.3	3.6	5.9	61	(51)
Eskimos [d]	1960	20	0.8	2.2	3.0	73	(29)
Volunteers given 3.5 mg per day orally [e]	1953–1954	2	30	3.9	34	11	(50)
Volunteers given 3.5 mg per day orally [f]	1957–1958	6	50	21	71	30	(55)
Volunteers given 35 mg per day orally [e]	1953–1954	6	234	24	258	9	(50)
Volunteers given 35 mg per day orally [f]	1957–1958	6	281	40	321	12	(55)

[a] All analyses were done using a colorimetric method.
[b] Not detected.
[c] Residents of the Wenatchee, Wash. area living within 500 ft of agricultural application.
[d] Alaskan eskimos who ate predominately a native diet shown to contain little or no DDT.
[e] Based on samples taken after 11 months or more of dosage.
[f] Based on samples taken after 21.5 months of dosage.

Since 1950, there have been many improvements in the analytical methods available for measuring DDT and related compounds. The first improvement introduced by Mattson and his colleagues [73] permitted the measurement of DDE through an adaptation of the classical Schechter-Haller colorimetric method.[97] DDE, which is one of the chief metabolites of DDT, had been entirely missed by earlier analytical methods. Later, the introduction of gas-liquid chromatography permitted chemists to distinguish the *o,p'*- and *p,p'*-isomers of DDT and DDE stored in human tissue and also to distinguish another metabolite, DDD. Furthermore, chromatography also permitted a more accurate measurement of DDE than was possible by the colorimetric procedure. At least in some series of paired samples, less total DDT-related material is found by gas chromatography than by the Schechter-Haller method because of a certain inherent inaccuracy of the older procedure.[20] However, the difference is small and not detectable at all in some sets of samples.[23] (See Table 5.)

Chlorinated hydrocarbon insecticides and fumigants are excreted in the milk of cows that ingest them.[48] Until recently, only DDT has been reported in human milk (Table 6),[25, 34, 62, 89, 107] but Egan *et al.*[34] reported that traces of BHC and dieldrin also were present. Recent studies of DDT in human milk [89] have revealed no increase since measurements were first made in 1950.[62] It is of interest that this milk contains more DDT than does cows' milk [34, 89] and that the mother is apparently in negative DDT balance during lactation.[89]

It was discovered in 1949 that DDT is transferred in dogs via the placenta to the fetus,[39] and this has been confirmed in rabbits,[67] mice,[7] and man.[25] It follows that we do not begin to reach a steady state of DDT storage after birth but rather are born—and probably conceived—with it. Dieldrin, too, is transferred to the fetus in mice.[7] In our own laboratory, W. E. Dale has found nine isomers and metabolites of six insecticides in the fat and organs of stillborns.

Several of the other chlorinated hydrocarbon insecticides were measured quite early in the tissues of people with heavy occupational exposure to the compounds or in people who had ingested formulations either through accident or with suicidal intent. However, it was not until the introduction of gas-liquid chromatography that it became possible to measure the small traces of chlorinated hydrocarbon insecticides other than DDT and DDE that occur in the general population (Table 7). The first report of this kind came from England.[58] The finding was soon confirmed,[34, 94] and

Table 5.
Concentration of DDT-Derived Material in Body Fat

Country	Year	No. of Samples	Analysis Method	DDT [a] (ppm)	DDE as DDT (ppm)	Total [b] as DDT (ppm)	DDE as DDT (% of total)	Reference
United States	1961–1962	28	Colorimetric	3.7	6.9	10.6	65	(20)
			GLC [c]	2.4	4.3	6.7	64	
France	1962–1963	5	Colorimetric	3.1	6.5	9.6	68	(53)
			GLC [c]	3.5	5.3	8.8	60	
India (Delhi area, civilian)	1964	24	Colorimetric	18	12	30	40	(23)
			GLC [c]	14.3	12.9	27.2	47	
India (other cities, military)	1964	11	Colorimetric	7	4	11	36	(23)
			GLC [c]	4.7	7.1	11.8	60	

[a] Includes *p,p'*- and *o,p'*-DDT.
[b] Includes all detected isomers of DDT and DDE, but not DDD.
[c] Gas-liquid chromatography.

Table 6.
Concentration of DDT-Derived Material in Human Milk

Country	Year	No. of Samples	Analysis Method	DDT (ppm)	DDE as DDT (ppm)	Total as DDT (ppm)	DDE as DDT (% of total)	Reference
United States	1950	32	Colorimetric	0.13	—	0.13	—	(63)
United States	1960–1961	10	Colorimetric	0.08	0.04	0.12	33	(89)
United States	1962	6	Colorimetric	0–0.12[a]	0.025[a]	<0.37[b]	—	(107)
Hungary	1963	10	Colorimetric	0.13–0.26[a]	—	—	—	(26)
England	1963–1964	19[c]	GLC[d]	0.05	0.08	0.13	62	(34)

[a] Range of values for milk containing 4 percent fat; milk fat contained 3.3 to 6.6 ppm.
[b] Maximum value.
[c] These samples also contained 0.013 ppm BHC and 0.006 ppm dieldrin.
[d] Gas-liquid chromatography.

Table 7.

Average Concentration of Chlorinated Hydrocarbon Pesticides (Other than Those Derived from DDT) in Body Fat of the General Population of Various Countries [a]

Country	Year	No. of Samples	Storage Level in Body Fat (ppm)				Reference
			BHC Isomers	Dieldrin	Endrin	Heptachlor Epoxide	
United States	1961–1962	28	0.20	0.15	[b]	[b]	(20)
United States	1962–1963	282	0.57	0.11 [c]	nd	[b]	(56)
United States	1964	64	[b]	0.31	<0.02	0.10	(112)
United States	1964	25	0.60	0.29	<0.03	0.24	(54)
England	1961–1962	131	[b]	0.21	[b]	[b]	(58)
England	1963–1964	65	0.42	0.26	[b]	<0.1	(34)
England	1964	100	0.02 [d]	0.21	<0.02	<0.01	(94)
France	1961	10	1.19	[b]	[b]	[b]	(53)
India	1964	35	1.43	0.04	nd	nd	(23)

[a] All analyses were carried out by gas-liquid chromatography.

[b] The specific pesticide was not tested for, or at least such testing was not mentioned in the published paper. If the pesticide was looked for but not detected, the result is shown as less than the sensitivity of the method used when this value is known; or, if the limit of sensitivity is not known, the result is simply shown as not detectable (nd).

[c] Only 64 samples were tested for dieldrin content.

[d] Only 20 samples were tested for BHC content.

it was shown that people in other countries,[23, 83] including the United States,[20, 54, 56, 112] store DDD, BHC, heptachlor epoxide, and dieldrin. Since DDD is an insecticide in its own right, as well as a metabolite of DDT, and since dieldrin in the tissues may be derived from aldrin as well as from preformed dieldrin, it follows that six insecticides or their metabolites have now been demonstrated in the adipose tissue of people from this country. The forms in which these six insecticides have been reported in fat from people of the general population of this or other countries are: *p,p'*-DDT, *o,p'*-DDT, *p,p'*-DDE, *o,p'*-DDE, *p,p'*-DDD, α-BHC, β-BHC, γ-BHC, heptachlor epoxide, and dieldrin.

Since only one chlorinated hydrocarbon insecticide, DDT, has been measured for a significant length of time, it is not yet possible to state whether people in this country have reached a steady state of storage for the other five compounds.

Robinson made a great forward step when he introduced a method capable of measuring dieldrin and the sum of DDT-related materials in human blood.[93] Early measurements of dieldrin in the blood of the general population were reported by Brown *et al.*[11] and by Kazantzis and his colleagues.[61] A further improvement in the analysis of insecticides in blood was introduced by Dale and his colleagues.[22] The new method gave results in good agreement with those of Kazantzis *et al.*[61] and Brown *et al.*,[11] but it also permitted the separate measurement of DDT and DDE, dieldrin, heptachlor epoxide, and β-BHC in the blood of people in the general population of this country. In fact, the method is capable of measuring any of the chlorinated hydrocarbon insecticides in human blood provided they reach a concentration of 0.0001 ppm or greater. The average concentrations actually measured in whole blood were: *p,p'*-DDT, 0.0058 ppm; *o,p'*-DDT, 0.0010 ppm; *p,p'*-DDE, 0.0114 ppm; β-BHC, 0.0031 ppm; dieldrin, 0.0014 ppm; and heptachlor epoxide, 0.0008 ppm.[22] In addition to the compounds found in the blood of the general population, *o,p'*-DDE, *p,p'*-DDD, γ-BHC, chlordane, aldrin, and toxaphene have been demonstrated in the blood of people with occupational or accidental exposure to these materials.[24]

The introduction of a method sufficiently sensitive to measure the traces of insecticide present in blood represents a marked advance over methods useful only for analysis of pesticides in fat because (a) it permits selection of samples from persons who should be studied because of the special conditions of their exposure to pesticides, and (b) there is some evidence that there

is a greater correlation between the concentrations of chlorinated hydrocarbon insecticides in blood and brain than there is between their concentrations in fat and brain.[21] This distinction is not important in connection with studies on the general population. In this group, the concentrations of pesticides in the fat are higher than those in any other tissue, and storage of the materials in fat shows an excellent correlation with dosage. However, in persons whose history of exposure to pesticides is imperfectly known and may include accidental exposure, blood samples should be analyzed because the results may be valuable for differential diagnosis.

So far, only a few measurements have been made of pesticides in human organs, and most of them were made in connection with recognized cases of fatal poisoning. Thus, high concentrations of DDT in the liver, kidneys, and heart of a poisoned person were reported as early as 1952.[68] Lindane at concentrations of 83 to 343 ppm was reported in the tissues of a child who died after eating one or more vaporizer tablets,[60] but much lower concentrations of 2.4 to 30.6 ppm were found in another child who died in the same way.[16] Endrin has been found at concentrations up to 10 ppm in the tissues of people poisoned by it.[46]

Only very recently it has become possible to detect chlorinated hydrocarbon insecticides in the organs of people who were presumably unaffected by them. The first such report was that of Radomski and Fiserova-Bergerova,[90] who found DDT, DDE, and dieldrin in most samples of brain, kidney, liver, and gonads that they analyzed. They also reported aldrin and lindane in a few of the samples. If one may judge from results on blood,[22] the finding of aldrin and γ-BHC and the failure to find β-BHC in tissue indicated that Radomski's subjects had some special exposure to pesticides and, therefore, were not typical of the general population. In our own laboratory, W. E. Dale has found traces of *p,p'*-DDT, *o,p'*-DDT, *p,p*-DDS, *o,p'*-DDE, *p,p'*-DDD, α-BHC β-BHC, γ-BHC, dieldrin, and heptachlor epoxide in the organs from people in the general population.

As we have seen, at least three inorganic and six chlorinated hydrocarbon insecticides or their metabolites are found regularly in people in the general population. In addition, at least nine other pesticides or their metabolites have been measured in persons with direct exposure to active material. For some compounds such as pentachlorophenol[38] and 2,4-D [(2,4-dichlorophenoxy) acetic acid],[19, 81] the values found so far have served only to estab-

lish dangerous or even fatal tissue levels. However, in other instances, it is practical to monitor workers to learn whether any are receiving excessive exposure, which, although not immediately harmful, should be reduced either through improved hygiene or through transfer of the worker to an entirely different kind of work. Such monitoring may be done best with blood samples for DNOC (4,6-dinitro-*o*-cresol).[86]

Significant absorption of any of the organic phosphorus or carbamate insecticides may be monitored through measurement of cholinesterase activity.[111] In the case of some organic phosphorus compounds, notably parathion [4, 85] and malathion,[52, 71] measurement of a metabolite in the urine has proved to be a more sensitive and reponsive test of absorption than measurement of blood cholinesterase. Elliott's test for paranitrophenol applies not only to parathion but also to methyl parathion and EPN (ethyl *p*-nitrophenyl phenyl phosphonate).

Exposure to a number of other pesticides may also be monitored through tests for metabolites in urine. The materials include lead,[58, 59] arsenic,[110] mercury,[99] carbaryl as 1-naphthol,[8] *p*-dichlorobenzene,[6, 47] and DNOC.[86] Significant occupational exposure to DDT may be monitored in this way (Table 8), but as shown by Durham *et al.*,[31] the present method for analysis of the urinary metabolite, DDA [bis (*p*-chlorophenyl) acetic acid] is not sensitive enough to permit satisfactory monitoring of the general population. In a similar way, it is practical to monitor workers with intense exposure to dieldrin by measuring some of its metabolites in urine.[17]

Relative Importance of Different Sources of Exposure

What is the relation between exposure and storage, especially for compounds found regularly in the general population? Animal studies have shown a close relationship between these two parameters for a wide range of pesticides. There is also a close relationship in man for DDT as shown by Figure 1, which is reproduced from a paper by Durham and his colleagues.[32] Evidence is still incomplete in connection with the other insecticides known to be stored in people, but there is no reason to suppose that they constitute an exception to the general rule.

Campbell and his colleagues estimated that over 90 percent of the DDT stored by the general population is obtained from food.[13]

Table 8.
Urinary Excretion of DDA by People in the United States with Varying Degrees of Exposure to DDT

Exposure	Year	No. of Samples	DDA Excretion (ppm)		Reference
			Range	Mean	
General population	1954	8	<0.05	—	(50)
General population	1957	8	<0.02–0.07	—	(55)
General population	1962	23	<0.02–0.18	—	(31)
Environmental [a]	1962	13	<0.02–0.11	—	(31)
Applicators	1962	11	<0.02–0.17	—	(31)
Formulators	1957	40	0.12–7.56	1.71	(85)
Volunteers given 3.5 mg per day orally	1953–1954	2	0.10–0.42 [b]	0.21 [b]	(50)
Volunteers given 3.5 mg per day orally	1957–1958	6	0.06–1.98 [c]	0.23 [c]	(55)
Volunteers given 35 mg per day orally	1953–1954	6	0.69–9.67 [b]	2.46 [b]	(50)
Volunteers given 35 mg per day orally	1957–1958	6	0.18–9.21 [c]	3.09 [c]	(55)

[a] Residents living within 500 ft of agricultural application.
[b] Based on all samples after 35th week of dosage.
[c] Based on all samples from the 35th through the 93rd week after dosage started.

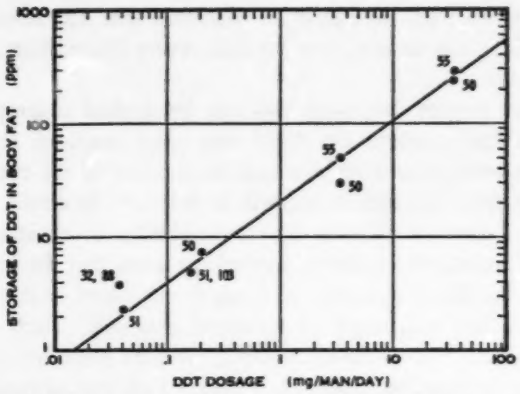

Figure 1. Storage of DDT in the body fat of people in relation to dosage. Numbers beside the points refer to references. (Reprinted from Durham *et al.*[32] by permission of the authors and the American Medical Association.)

This is consistent with the measured intake from food and water listed above, that is 0.04 mg per man per day from food and less than 0.000046 mg per man per day from water. It is also consistent with the fact that, at most, only traces of DDT have been measured in air except the air of work places. The average concentration of DDT in the air of small communities in heavily sprayed agricultural areas would determine an intake of 0.0002 to 0.0008 mg per man per day according to Tabor.[101] Antommaria *et al.* found an even lower average concentration in the air of a large city determining an intake of about 0.000009 mg per man per day.[3] Durham *et al.* reached the same conclusion by pointing out the close relationship between DDT intake in food and its storage in fat.[32] One may conclude from their data that any stored DDT derived from sources other than food is too small to be distinguished by present chemical methods. For the general population, the only important route of exposure to pesticides is the oral route, and the only important source of exposure is food. The situation is entirely different for persons with accidental or occupational exposure. The source of exposure in these instances may be formulations of the compound or residues of it on surfaces. In nonoccupational accidents, exposure is usually oral; occupational exposure is usually respiratory, dermal, or both.

Critique of Safety

The only assurance we have for the safety of pesticides, drugs, or foods is the dosage–response relationship. Even materials of

low toxicity such as aspirin or materials that are necessary to life such as salt or water can produce severe intoxication or death if misused.

Under present law, pesticides can be applied to crops or to animals that produce our food only after extensive studies in animals have given assurance that the amount of the compounds that we may eventually ingest will be safe.[1, 62] However, because species frequently differ in their susceptibility to chemicals, it is wise to monitor their effects, particularly when they are first introduced. Studies in man may be made in volunteers or in men with intensive and prolonged occupational exposure. Each kind of study has its own special advantages, but both contribute information on the possible effects of relatively high and sustained rates of absorption.[79] Volunteers tolerated 35 mg of DDT per man per day for periods of 21 months without any detectable effect except the increased storage and excretion of the compound and its derivatives. Workers in formulating plants have tolerated approximately the same rate of absorption for longer periods.[83] These dosage rates of 35 mg per man per day in volunteers and workers represent a DDT intake about 200 times greater than that measured in restaurant meals in 1953 and 1954 [103] and about 970 times greater than the average measured in 1962 by Durham *et al.*[32] In considering the future safety of workers who continue to be employed in the formulation of DDT, one must depend largely on animal experiments. Rats withstand a daily dosage at least 10 times that of these workers without any detectable clinical effect,[40, 84] although minimal reversible tissue change may be present.[84] Dogs [84] and monkeys [80] also withstand a daily dosage 10 times greater than that of the workers, but they do not show the tissue changes, which seem to be peculiar to rats. Although one cannot predict the future safety of workers from their present tolerance for DDT, one can use the experience already gained to predict the future safety of the general population in relation to DDT. It has been shown for at least two animal species that toxicity resulting from a lifetime of exposure is seldom very different from toxicity resulting from 90 days of exposure at the same dosage rate.[106] The largest factor of difference observed was 20. Ninety days constitute about one eighth of the life-span of a rat. Many workers have now been exposed to DDT for much more than one eighth of their life-span. Since they have not suffered detectable harm, it seems most unlikely that the general population will be harmed by dosages 200 to 970 times smaller than those to which the workers are exposed.

The other chlorinated hydrocarbon insecticides have not been studied in man as thoroughly as DDT. However, information on some of them, especially dieldrin and methoxychlor, are collecting rapidly. It is already clear that the same general conclusions will apply, although the exact factors of safety may be different.

Eventually, it will be necessary to take all values into account. The chlorinated hydrocarbon insecticides, especially DDT, have a good safety record although they are tenaciously stored. As they are replaced by compounds that are less stored, there may be an increased hazard to workers. In fact, there has already been an increase in deaths caused by the more toxic organic phosphorus insecticides.

Future Research

It may be predicted that, as monitoring of pesticides continues, additional compounds will be found both in food and in human tissue. This is partly because some compounds have not been looked for and partly because improved chemical methods continue to be developed. It is almost certain that a number of chlorinated hydrocarbon insecticides occur in the fat and blood of people in the general population at levels too low to be detected by the best methods now available.

The lively interest that now exists in pesticides is evidenced in part by the monitoring programs sponsored by the FDA, the U.S. Public Health Service, the U.S. Fish and Wildlife Service, and the U.S. Department of Agriculture. All of these are concerned, at least in part, with food. That of the Public Health Service is concerned with people also. Even though fish and wildlife contribute only a small proportion of our food, it seems likely that some information bearing on human health will also be obtained from the monitoring program concerned with these forms. The nature and extent of these official programs has been announced recently,[2] and they are the subject of other reports.[33, 43] In addition to the official monitoring programs, it seems likely that some private efforts along this line will continue as in the past.

Important as it is to monitor the general population, those responsible for this work should keep it in perspective. First, it is also important to measure the storage of people with heavy and persistent occupational contact with any material to which the general population is exposed. Such a study can usually be made for any synthetic compound and for any other materials, such as the heavy metals that are used in industry. It may be difficult to

find distinct populations with high exposure to naturally occurring materials that have no industrial use.

It is also important to establish the major sources of exposure in each situation. Different populations and different compounds need not be identical in this respect. For example, respiratory exposure to lindane may be highly important only if it is used in vaporizers.

There is a certain temptation to measure what is known. Quinby and his colleagues showed that in the measurement of DDT in fat it was possible to achieve a precision of approximately 55 percent by using only 10 samples to estimate the average storage.[88] Even this low precision was adequate to distinguish storage of DDT in people with unusual dietary habits or in people with moderate occupational exposure from storage in people of the general population. It may be of greater importance to obtain an approximate measurement of the storage of a wide range of compounds than to obtain a very exact measurement of the storage of a few materials.

In view of the intense hepatotoxic and carcinogenic action of the aflatoxins, it would seem difficult to overestimate the importance of their study. The same may be true of other fungal toxins and perhaps a wide range of compounds of plant origin.

Eventually, toxicologists must take responsibility for answering the question "How important?" as well as the question "How much?" Naturally occurring toxins cannot be ignored, particularly since they are the only ones that might have contributed to diseases that occurred before the modern pesticides were invented.

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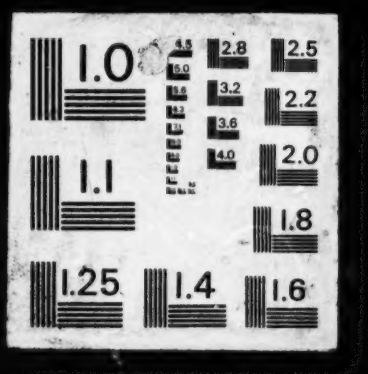

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Levels of Polychlorinated Biphenyls in Adipose Tissue of the General Population of the Nation

PESTICIDE
PUBLICATION

523

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Polychlorinated biphenyls (PCBs) have been reported in many different parts of the environment in this country (1-3). The purpose of this report is to present preliminary results from a monitoring program in which these materials are routinely sought and quantitated.

The Human Monitoring Survey, established in 1967 by the Pesticides Program, DHEW (now Division of Pesticide Community Studies, EPA), determines, on a continuing basis, the exposure to pesticides experienced by the general population by measuring levels of pesticide residues present in tissues or excreted in urine. Initially, technological limitations and resource restrictions limited the Survey to the identification and measurement of those chlorinated hydrocarbon residues which are stored in measurable amounts in mammalian adipose tissue, or which can be measured in blood, these residues being a reflection of past exposure. The initial program plan has been and continues to be reviewed frequently with reference to technological and/or research developments to identify other groups of pesticides and other materials of interest, which can be incorporated with slight modification of the existing program.

Samples are collected through the direct cooperation of pathologists, who are in hospital or private practice or who are in public service as city or county medical examiners. Samples are collected from both sexes in all age and racial groups. Adipose samples are collected from tissues removed for therapeutic surgery or from postmortem examinations, the latter including people who have died accidentally (trauma) or during relatively brief hospitalization. No samples are accepted from institutions for long-term care of the chronically ill patient.

All samples are analyzed by laboratories established under contract with State Health Departments or at community study projects in Michigan, Florida and Colorado. These laboratories use analytical methodologies specified by the program on the advice of technical consultants and are required to maintain acceptable levels of performance, as demonstrated in both inter- and intra-laboratory quality control programs. Technical consultation for analytical aspects of the Survey is provided by the Chemistry Branch, Perrine Primate Laboratory, EPA, under the direction of Henry F. Enos, Ph.D., Chief.

In 1969, with the increased interest in polychlorinated biphenyls, it was recognized that PCBs probably occur in several segments of the environment and that their presence would distort analytical values for certain pesticides, especially selected DDT residues. The monitoring laboratories were therefore asked to report all samples suspected of containing PCBs by gas-liquid chromatography. A reporting system was developed based on rough quantitation, as follows: negative, present in usual amounts, present in greater or lesser amounts than usual. Samples collected in late 1968 and 1969 showed that PCBs were indeed present in a significant portion

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of the general population of the country over a wide geographic distribution. Positive samples were reported from 14 States, including Michigan, New York, Minnesota, California, Massachusetts, Georgia, Kentucky, Illinois, North Carolina, South Dakota, Ohio, Louisiana, Delaware and Arkansas. To insure that proper identification was being made, two samples with higher levels were confirmed by combined gas liquid chromatography-mass spectroscopy (4). These two cases are discussed in another paper in this symposium (5).

Based on these preliminary findings and certain as yet unpublished information about the effect of PCBs on the accuracy of measurement of residues of DDT (Enos, H. F., personal communication), high priority was given by the Perrine Laboratory to the development and evaluation of an analytical method which would separate PCBs from pesticides permitting accurate quantitation of pesticides and confirmation of PCB levels. The resulting methodology is a further modification of the Mills-Olney-Gaither procedure in which adipose tissue is subjected to extraction by petroleum ether, acetonitrile partitioning, and Florisil cleanup. A portion of the resulting 6% ethyl ether/petroleum ether eluate, in concentrate form, is treated with KOH to effectuate dehydrochlorination of DDT and DDD to their olefins, thus eliminating the problem of separating these pesticides from the PCBs. Oxidative treatment is then applied to convert any interfering DDE to p,p'-dichlorobenzophenone which has an Rf value different from the PCBs. The PCBs are then determined by thin layer chromatography (6).

On April 15, 1971, all monitoring laboratories in the Human Monitoring Survey adopted this methodology for the analysis of all adipose samples with the lowest limit of sensitivity being 1.0 ppm. Aliquots of all samples in which measurable amounts of PCBs are found are saved for future confirmation by mass spectroscopy.

Table 1. Incidence of polychlorinated biphenyls in adipose of the general population of the nation.

	Reported		Analyzed	
	No.	%	No.	%
Total	637	100.0	688	100.0
Negative	314	49.3	235	34.2
Trace–<1.0 ppm	125	19.6	229	33.3
1–2 ppm	165	25.9	188	27.3
>2 ppm	33	5.2	36	5.2

Table 2. Descriptive statistics of samples analyzed.

		Negative and trace–<1.0 ppm		>1.0 ppm	
		No.	%	No.	%
Total number		439	100.0	198	100.0
Sex					
Male		221	50.3	127	64.1
Female		218	49.7	71	35.9
Race					
White		381	86.8	151	76.3
Nonwhite		58	13.2	47	23.7
Samples from					
Therapeutic surgery		95	21.6	29	14.6
Postmortem		344	78.4	169	85.4
Diagnostic group					
Neoplasms	140–209	77	17.5	39	19.7
Circulatory system	390–450	121	27.6	61	30.8
Gastrointestinal system	530–565	44	10.0	16	8.1
Liver & gall bladder	570–575	20	4.6	6	3.0
Pancreas	577	0	0.0	2	1.0
Urinary system	580–595	11	2.5	7	3.5
Congenital Anomalies	740–759	5	1.1	1	0.5
Accidents & violence	E numbers	16	3.6	7	3.5
All other		145	33.0	59	29.8
		439	99.9	198	99.9

Results and Discussion

Analytical results for 637 samples have been reported and are summarized in Table 1 (51 additional samples have been analyzed but have not as yet been reported). Of the 637 samples reported, 198 (31.1%) contained measurable amounts of PCBs and 125 (19.6%) contained trace amounts, with the balance being negative. These samples were collected from 40 pathologists in 38 cities distributed over 18 States and the District of Columbia. The States are Arkansas, Illinois, Louisiana, Oklahoma, South Dakota,

Tennessee, Oregon, Pennsylvania, Florida, Kansas, Maine, Georgia, North Carolina, California, Michigan, New York, Ohio and Kentucky. Positive samples came from every hospital, city and state sampled. It, therefore, appears that these materials are widely found in the population. Details of distribution by sex and race, collection procedure, and diagnostic groups are summarized in Table 2. The difference between figures for the positive and negative groups does not appear to be significant, although no statistical evaluation has been attempted because of the preliminary nature of this report. Since a statistical design has been established and is being followed for sample collection for the Human Monitoring Survey, in due time valid statistical analysis will be possible and will then be performed.

Summary

Polychlorinated biphenyls have been found in measurable amounts in 31.1% of 637 samples of human adipose tissue collected from the general population as a part of the Human Monitoring Survey. Sample collection involved 18 States and the District of Columbia. Positive samples were obtained from every State sampled.

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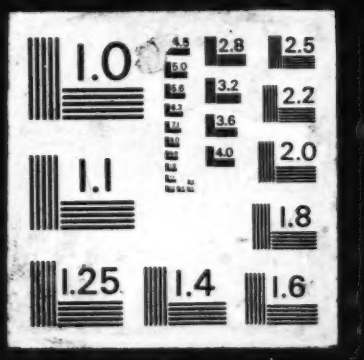

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RESIDUES OF POLYCHLORINATED BIPHENYLS IN THE GENERAL POPULATION OF THE UNITED STATES

Frederick W. Kutz, Ph.D., and S. C. Strassman*

Abstract

Residues of polychlorinated biphenyls have been found in human adipose tissue and in milk collected from the general population of the United States. In a national survey of human adipose tissue during fiscal years 1973 and 1974, 35.1 and 40.3 percent, respectively, of the tissue collected contained levels of 1 ppm or more of polychlorinated biphenyls on a wet-weight basis. Electron capture-gas chromatographic analysis of this tissue revealed that the compounds found in adipose tissue were most comparable to those prevalent in Aroclor 1254 and Aroclor 1260. Additionally, semiquantitative estimation of these residues was accomplished by thin-layer chromatography. Evidence from gas-liquid chromatography-mass spectrometry indicated that the most frequently encountered polychlorinated biphenyl residues were penta-, hexa-, and heptachlorobiphenyl compounds.

Human milk samples collected in selected counties of Arkansas and Mississippi were found to contain trace quantities (<1 ppm) of polychlorinated biphenyls on a wet-weight basis.

Human exposure to polychlorinated biphenyls may come from direct contact with industrial products containing these compounds, from association with contaminated environmental components or from many combinations of the two. Intake of these compounds may occur by three routes: (1) ingestion, (2) respiration, and (3) absorption through the skin and mucous membranes. Most probably, all contribute to the total body burden of these chemicals; none of these routes of exposure can now be identified as the most important.

Polychlorinated biphenyls have been found in human adipose tissue collected for the National Human Monitoring Program as reported by Yobs (ref. 1). This program is a continuing ambient monitoring activity which functions to determine, on a national scale, the exposure of the general population to pesticides and to assess changes in these parameters when they occur. Polychlorinated biphenyls, in addition to certain organochlorine pesticides, are detected in human adipose tissue following a multiresidue analytical procedure stipulated by the National Human Monitoring Program for Pesticides.

The objective of this paper is to report the findings of polychlorinated biphenyls during the human monitoring surveys conducted in fiscal years 1973 and 1974. These results are compared to those obtained in the 1971 survey. Additionally, the results of the analysis of human milk for polychlorinated biphenyls are presented. Data from gas-liquid chromatography-mass spectrometric analysis of the polychlorinated biphenyls in human adipose tissue and milk are also reported.

Early confirmation of polychlorinated biphenyls in human depot fat was accomplished in 1967 by Widmark (ref. 2) using combined gas chromatography mass spectrometry. An article by Biros et al. (ref. 3) reported that two human adipose tissues examined by combined gas chromatography mass spectrometry were shown to contain substantial quantities of polychlorinated biphenyls ranging from pentachlorobiphenyl to decachlorobiphenyl and included at least 14 isomers and chlorine homologs. These samples, supplied by the National Human Monitoring Program for Pesticides, were selected because of indications of unusually high levels of these chemicals.

One of the laboratories routinely engaged in human tissue analysis, under contract to the National Human Monitoring Program for Pesticides, published data regarding the polychlorinated biphenyl content of human adipose tissue (ref. 4). According to this study, 41 to 45 percent of the general population had levels of 1 ppm or more of polychlorinated biphenyls with isomers contained in Aroclors 1254, 1260, 1262, and 1268. The presence of these compounds, ranging from pentachlorobiphenyl to decachlorobiphenyl, was confirmed in three samples by combined gas chromatography mass spectrometry.

Polychlorinated biphenyls were found in measurable amounts in 31.1 percent of 637 samples of human adipose tissue collected from the general population as part of the Human Monitoring Survey during 1971 (ref. 1). Sample collection involved 18 states and the District of Columbia. Positive samples were obtained from each political jurisdiction sampled.

Residues of these compounds have also been detected in other human tissues and milk. In a study of human milk collected in Colorado, 8 of 40 samples contained residues of polychlorinated biphenyls ranging from 40 to 100 ppb (ref. 5).

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METHODS AND MATERIALS

Samples of adipose tissue from individuals of the general population were obtained through the cooperation of pathologists and medical examiners in 75 selected collecting sites throughout the contiguous 48 States.

Sampling: A stratified random design, with sampling proportioned to populations, was followed for selecting cities in which tissue samples were collected. The strata were the nine census divisions as designated in the 1970 Census; the sampling units in each census region were cities with populations in excess of 25,000 people. The number of cities designated within each census division was based on population. The cities which served as collecting sites are shown in figure 1.

This design provided samples which are statistically representative of the general population. For each collection site, an annual sample quota was established to reflect the demographic distribution in that census division. The sample quota in each of these groups was allocated proportionally according to the age, sex, and race distribution, as determined by the 1970 Census.

Adipose tissue was collected by cooperating pathologists and medical examiners from postmortem examinations and from specimens which had been removed during therapeutic surgery. Thus, tissues were received from patients having pathological conditions as well as those dying from sudden acute illness or from trauma. Information recorded for each tissue sample included age, sex, race, and pathological diagnosis. Geographic residence was assumed to be in the general location of the hospital. Since the objective of the program was to reflect the pesticide and other pollutant burden in the general population, samples were not collected from cases in which a diagnosis of pesticide poisoning was suspected or known, from cachectic patients, or from patients who had been institutionalized for extended periods. Further details of the program were presented by Yobs (ref. 6).

Chemical Analysis: Samples were analyzed chemically by contract laboratories using only methodologies specified by the program. All laboratories were required to maintain acceptable performance levels in an interlaboratory quality assurance program established and moderated by the EPA Pesticides and Toxic Substances Effects Laboratory, Research Triangle Park, N.C. 27711. This laboratory also provided technical assistance for the analytical portion of the program.

Samples were analyzed for selected chlorinated hydrocarbon insecticides (table 1), and polychlorinated

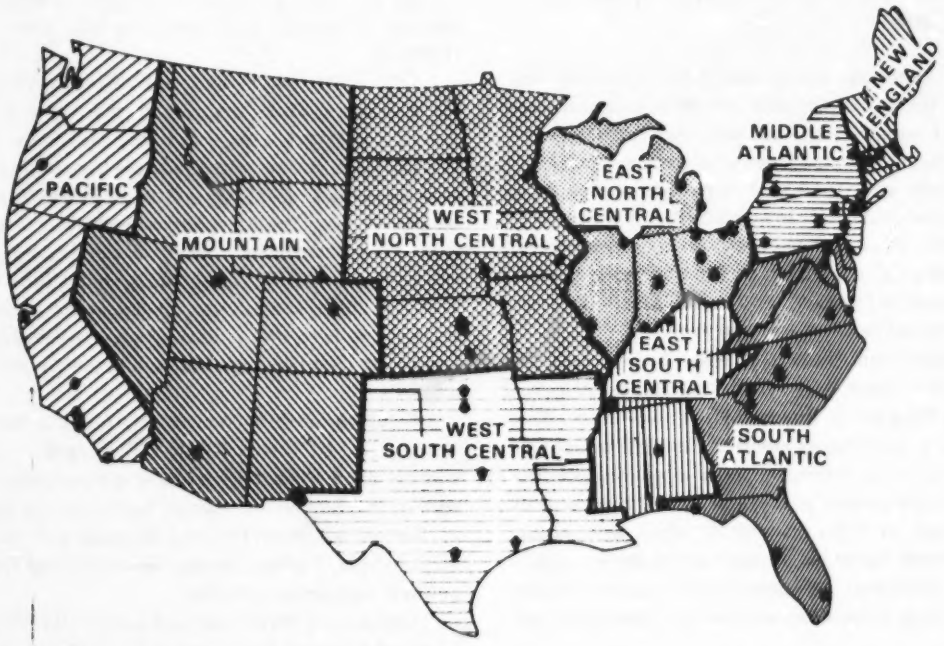

Figure 1. Map of the United States showing census divisions and collection sites for the National Human Monitoring Program for Pesticides.

Table 1. List of chemicals detectable in human adipose tissue

o,p'-DDT	aldrin
p,p'-DDT	dieldrin
o,p'-DDE	heptachlor
p,p'-DDE	heptachlor epoxide
o,p'-DDD	endrin
p,p'-DDD	mirex
α-BHC	oxychlordane
β-BHC	trans-nonachlor
lindane	polychlorinated biphenyls
δ-BHC	hexachlorobenzene

biphenyls, using a modified Mills-Olney-Gaither procedure (ref. 6). Gas-liquid chromatography with electron capture detection was employed for basic compound identification and quantification. The analytical determinative procedure for polychlorinated biphenyls in tissue involved: (a) extraction, partitioning, and Florisil column chromatographic purification of the residues together with the chlorinated hydrocarbon pesticides present in the tissue sample, and (b), thin layer chromatographic (TLC) semiquantitative estimation of residues in the purified extract following elimination of interferences from *o,p'*- and *p,p'*-DDE, DDD, and DDT residues by chemical conversion to the respective isomer of dichlorobenzophenone. The details of the TLC procedure included treatment of the extract with ethanolic potassium hydroxide to effect dehydrochlorination of DDT and its analogs to DDE. This was followed by oxidation with chromium trioxide in acetic acid to convert DDE residues to dichlorobenzophenone, which may be conveniently separated from the polychlorinated biphenyl residues by the TLC procedure. The plates were coated with silver nitrate-impregnated aluminum oxide G and developed with 5 percent benzene in hexane. Ultraviolet visualization of the eluted polychlorinated biphenyl residues and semiquantitative comparison of sample spot intensity with those observed for standard materials completed the polychlorinated biphenyl determination.

A total of 140 human adipose tissue sample extracts from the general population have been subjected to analysis by combined gas chromatography-mass spectrometry (GC-MS) to confirm and identify polychlorinated biphenyl components stored in human tissue. Levels of total polychlorinated biphenyls in the samples based on TLC determination ranged from 0.4 to 3.5 ppm. The adipose tissue samples had been extracted and subjected to the purification procedures described earlier. Conversion of the DDT-type residues to dichlorobenzophenone was effected by the combined dehydrochlorination, oxidation, chemical procedures. A final Florisil column chromatographic step was included to further purify the polychlorinated biphenyl residues and remove the dichlorobenzophenones present at relatively high levels in the extract.

RESULTS AND DISCUSSION

The levels of polychlorinated biphenyls found in general population samples of adipose tissue during fiscal years 1973 and 1974 are presented in table 2. Results presented by Yobs (ref. 1) are included for comparative purposes. During fiscal years 1973 and 1974, 35.1 and 40.3 percent, respectively, of the tissues collected contained levels of 1 ppm or more of polychlorinated biphenyls on a wet-weight basis. These frequencies are slightly higher than the 32.5 percent figure reported by Yobs (ref. 1) and are slightly lower than those (41-45 percent) reported by Price and Welch (ref. 4). The percentage of tissues which contained quantifiable amounts of polychlorinated biphenyls appears to be remaining relatively constant. However, there does seem to be an increase in the percentage of tissues which contained trace levels of this chemical although the limit of detection (1 ppm) remained constant. It should be interesting to determine whether these trace values will be converted to quantifiable amounts as the exposure of the general population continues over time.

National frequencies for fiscal years 1973 and 1974 were compared to frequencies for each census division and are presented in figure 2. The New England, Middle Atlantic, South Atlantic, and East North Central Census Divisions had frequencies of quantifiable levels exceeding the national frequencies for both survey years. The Mountain and East South Central Census Divisions had levels higher than the national levels for one survey year and lower for the other survey year. The Pacific, West North Central, and West South Central had levels lower than the national levels for both survey years.

Table 2. Levels of polychlorinated biphenyls in human adipose tissue

Data source	Sample size	Percent nondetected	Percent < 1 ppm	Percent 1-2 ppm	Percent > 2 ppm
Yobs, 1972	688	34.2	33.3	27.3	5.2
FY 1973 Survey	1277	24.5	40.2	29.6	5.5
FY 1974 Survey	1047	9.1	50.6	35.4	4.9

Figure 2. Map of the United States depicting census divisional frequencies of polychlorinated biphenyls.

The most frequently encountered polychlorinated biphenyl residues in the human adipose tissue extracts examined by combined gas chromatography-mass spectrometry were the penta-, hexa- and heptachlorobiphenyl compounds.

As polychlorinated biphenyls enter a biological system, the less chlorinated isomers are apparently either metabolized or excreted. These biochemical reactions alter the original Aroclors, so that electron capture chromatograms of these compounds from biological systems do not exactly match available laboratory reference standards. However, it can be noted that results do indicate that the polychlorinated biphenyls found in human adipose tissue most closely resemble Aroclor 1254 and Aroclor 1260.

The National Human Monitoring Program also collected and analyzed 57 samples of human milk from selected areas of Arkansas and Mississippi. The survey design was related to rice culture areas in which the herbicide 2,4,5-T was used. All of these samples contained trace amounts of polychlorinated biphenyls, the presence of which were confirmed by combined gas chromatography-mass spectrometry in a composite sample.

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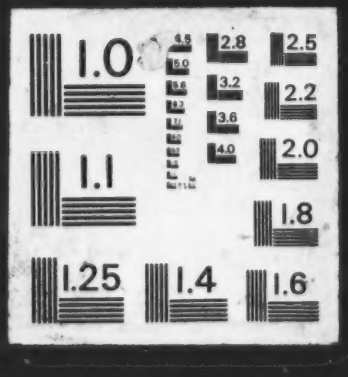

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PUBLICATION

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DDT IN HUMAN MILK

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IN 1950, Laug *et al.* investigated the DDT excretion-level in human milk in the United States[1]. These workers found DDT in 30 of 32 samples (94 per cent) of milk from women in Washington, D.C., with no recognized exposure to this insecticide other than that of the general population. The average concentration of DDT in these samples was 0·13 p.p.m. with a range of zero to 0·77 p.p.m. In 1962, tests on six individual samples and one pooled sample of human milk in California showed DDT-levels ranging from zero to 0·12 p.p.m. and DDE contents from none to 0·25 p.p.m.[11]. The highest total of DDT and DDE was 0·37 p.p.m. In Hungary, the milk of ten healthy nursing mothers was found to contain from 0·13–0·26 p.p.m. of DDT in whole milk or 3·3–6·6 p.p.m. in the lipid fraction[2].

This article reports the excretion of DDT in human milk as measured in individual and pooled samples collected in several cities in the United States during 1960 and 1961. The work is a component part of a more comprehensive study. The complete project involves determination of DDT and DDE storage-levels in body fat and DDA excretion rates in urine for the general population and for specific environmental and occupational groups as well as measurement of DDT and DDE content of complete prepared meals. These surveys have been correlated by obtaining as many of the samples as possible from the same individuals. For example, a number of the subjects in the work recorded here also contributed meals from their households for study of DDT and DDE ingestion rates. The results of the other segments of the complete DDT study will be published separately[3–5].

A total of 10 individual and 4 pooled samples of human milk were analysed. The individual samples were collected in Chicago, Illinois (4 donors), Wenatchee, Washington (5 donors), and Phoenix, Arizona (1 donor). Multiple samples representing time-periods varying from 2 to 7 months were collected from three of the donors in Chicago to determine the temporal variation in the concentration of DDT and DDE. The pooled samples were collected by the Fitzsimmons Army Hospital in Denver, Colorado. These samples were pooled from many (13 to 44) donors

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who were dependants of military personnel from various parts of the United States.

The samples from Chicago and Denver were obtained as the precipitate formed by the treatment of 1–2 l. of formalized milk using the method of Murthy *et al.*[6]. The filtrates had been used for determination of strontium-90 levels. These precipitates were provided through the courtesy of the Robert A. Taft Sanitary Engineering Center, Cincinnati, Ohio. The samples from Wenatchee and Phoenix were frozen as whole milk in plastic bottles until analysis. The sample from Phoenix had been formalinized prior to freezing.

Complete histories of exposure to pesticides were obtained from the donors of the individual milk samples. Three of the donors from Wenatchee lived in houses immediately adjacent to orchards that had been periodically treated with DDT for many years. However, no DDT was applied to these orchards during the period of milk collection. None of the other donors had any known exposures to DDT otner than those characteristic of the general population (that is, consumption of small amounts of residue in the diet and occasional household use of sprays or aerosols containing DDT). It was not practicable to obtain the histories of exposure to pesticides from the women who contributed to the four pooled samples.

Aliquots (usually 100 ml. of milk) were analysed by a modification of the Schechter-Haller spectrophotometric method[7]. Even though the limited accuracy of this method for quantities of DDT and DDE less than 5 μg was realized, all samples which produced recognizable Schechter–Haller colours were accepted at their calculated values. In all but three of the samples analysed, visible blue, red, or intermediate colour was produced in the Schechter-Haller reaction.

All the values given in this article for total DDT-derived material (DDT plus DDE) have been expressed in terms of DDT equivalent. Numerically this is accomplished by multiplying DDE concentration by the factor 1·11. Values for DDE expressed as a fraction of total DDT-derived material were determined by use of the following formula:

$$\text{DDE (\% of total)} = \frac{\text{DDE (p.p.m. as DDT equiv.)}}{\text{DDE (p.p.m. as DDT equiv.)} + \text{DDT (p.p.m.)}}$$

Recent investigations have indicated that gas chromatographic techniques are able to detect smaller quantities of DDT and DDE and to distinguish more quantitatively the various isomers and ratios of isomers than is the colorimetric procedure[8]. Nevertheless, the Schechter-Haller method has been used for so long that it is important for purposes of comparison with earlier investigations for

Table 1. Concentration of DDT and DDE in Human Milk in the United States

Type of sample	Location	Donor No.	Whole milk				Lipid fraction			DDE (% of total)
			Lipid content (%)	DDT (p.p.m.)	DDE as DDT (p.p.m.)	Total as DDT (p.p.m.)	DDT (p.p.m.)	DDE (p.p.m.)	Total as DDT (p.p.m.)	
Individual	Chicago, Illinois	1	3·63	0·09	0·09	0·18	2·5	2·2	4·9	50
		2	2·85	0·13	0·04	0·17	4·6	1·4	6·1	25
		3	2·83	0·09	0·02	0·11	3·2	0·7	4·0	20
		4	2·63	0·08	0·08	0·16	3·0	2·7	6·0	49
		Mean	2·99	0·10	0·06	0·16	3·3	1·7	5·3	36
Individual	Wenatchee, Washington	5	1·80	< 0·01	< 0·01	< 0·02	< 0·6	< 0·6	< 1·3	—
		6	5·81	0·07	0·01	0·08	1·2	0·2	1·4	14
		7	4·09	< 0·01	< 0·01	< 0·02	< 0·3	< 0·3	< 0·5	—
		8	3·29	< 0·01	< 0·01	< 0·02	< 0·3	< 0·3	< 0·6	—
		9	2·87	0·22	0·14	0·36	7·7	4·5	12·7	40
		Mean	3·57	0·06	0·03	0·09	2·0	1·2	3·3	39
Individual	Phoenix, Arizona	10	3·26	0·06	0·03	0·09	1·8	0·9	2·9	36
Individual	Mean for all individual samples		3·31	0·08	0·04	0·12	2·5	1·4	4·0	38
Pooled	Denver, Colorado, and other cities	Pool *A*	1·56	0·05	0·07	0·12	3·2	3·9	7·5	57
		Pool *B*	1·83	0·07	0·12	0·19	3·8	6·0	10·5	64
		Pool *C*	2·14	0·08	0·11	0·19	3·7	4·7	8·9	58
		Pool *D*	1·79	0·06	0·09	0·15	3·3	4·5	8·2	61
Pooled	Mean for all pooled samples		1·83	0·07	0·10	0·17	3·5	4·8	8·8	60

Table 2. Temporal Variation in Concentration of DDT and DDE in Human Milk

	Donor I		Donor II		Donor III	
	DDT (p.p.m.)	DDE (p.p.m.)	DDT (p.p.m.)	DDE (p.p.m.)	DDT (p.p.m.)	DDE (p.p.m.)
Monthly	0·08	0·07	0·09	0·02	0·13	0·04
replicates	0·07	0·06	0·10	0·05	0·14	0·03
	0·04	0·03	0·10	0·04		
	0·05	0·08	0·09	0·04		
	0·06	0·06	0·12	0·16		
	0·03	0·04	0·12	0·07		
			0·12	0·09		
Mean	0·06	0·06	0·11	0·07	0·14	0·04

some additional data to be collected in this way, at least until there is more information based on the newer techniques[9].

The concentrations of DDT and DDE in these samples of human milk are shown in Table 1. Whole milk contained an average of 0·08 p.p.m. DDT and 0·04 p.p.m. DDE based on the individual samples and 0·07 p.p.m. DDT and 0·10 p.p.m. DDE based on the pooled samples. The lipid fraction contained an average of 2·5 p.p.m. DDT and 1·4 p.p.m. DDE based on the individual samples and 3·5 p.p.m. DDT and 4·8 p.p.m. DDE based on the pooled samples. There is good correspondence between the DDT levels for these two types of samples; however, the DDE levels correlate less closely.

Data collected in the survey recorded here on the variation in the excretory level of DDT and DDE in human milk over a period of time is shown in Table 2. It can be seen that there was little change in the excretory levels of DDT and DDE for each individual subject over the 2–7-month periods investigated.

The trend in the concentration of DDT in human milk in the United States between 1950 and 1960–61 is illustrated in Table 3. The mean DDT concentration was 0·13 in 1950 as compared with 0·07–0·08 p.p.m. in 1960–61. A comparison of the frequency distribution shows that there were fewer samples at the higher concentration levels in the later survey. Results of the earlier survey

Table 3. Trend in the Concentration of DDT in Human Milk in the United States

Range of values (p.p.m. of DDT)	Percentage of samples		
	1950 (Laug *et al.*)	1960–61 (this paper) Individual	Pooled
< 0·01	6	30	0
0·01–0·05	9	0	25
0·06–0·10	25	50	75
0·11–0·15	41	10	0
0·16–0·20	6	0	0
0·21–0·30	6	10	0
0·31–0·40	0	0	0
0·41–0·50	3	0	0
> 0·50	3	0	0
Total No. of samples	32	10	4
Mean concentration (p.p.m.)	0·13	0·08	0·07

were not reported on the basis of lipid fraction nor was the DDE content of the milk determined. The range of values in the work reported here for both DDT (< 0·01–0·22 p.p.m.) and DDE (< 0·01–0·14 p.p.m.) is comparable with that for samples collected in California in 1962 (DDT, zero to 0·12 p.p.m.; DDE, zero to 0·25 p.p.m.)[11].

It is of interest to compare the DDT and DDE levels in the fat moiety of human milk samples with the storage levels of these compounds in human body fat. In a recent investigation using analytical techniques comparable with those used in the work recorded here, storage levels of 6·8 p.p.m. DDT and 13·5 p.p.m. DDE in the extractable lipid fraction of human body fat taken from persons in the general population of the United States were found[3]. Thus, although concentrations in both tissues are of the same order of magnitude, DDT, and particularly DDE, levels appear to be somewhat lower in the fat moiety of human milk than in the extractable lipid fraction of human body fat. In the body fat, DDE represented 68 per cent of the total DDT-derived material, while in the milk DDE constituted 38 per cent (based on individual samples) or 60 per cent (based on pooled samples) of the total. The DDT levels in human milk from Hungary (3·3–6·6 p.p.m. in the lipid fraction)[3] are associated with an average DDT storage level in human body fat in that country of 5·7 p.p.m.[10].

Apparently, Hungary is the only country other than the United States for which values for DDT excretion in human milk have been reported. The values from Hungary for DDT in human milk (0·13–0·26 p.p.m. in whole milk) appear to be somewhat higher than the levels reported here or those reported by West[11] for the United States. In comparing DDT storage levels in human body fat from various countries, Quinby *et al.*[3] concluded that the level in Hungary equalled or exceeded that in the United States, while the concentrations were lower for other countries (Canada, Britain, France, and Western Germany) for which data were available.

The pharmacodynamic relationships of DDT intake, storage and excretion are incompletely understood, even in physiological situations in which the complicating factors involved in lactation do not occur. However, it can be calculated that a daily output of 700 g of milk containing 0·07 p.p.m. of DDT would account for a total daily excretion of about 0·05 mg of DDT by this route. This amount would account for about 125 per cent of the estimated daily dietary intake of DDT for the general population of this country (0·04 mg/person/day)[5]. Another fraction of the intake is excreted in the urine as DDA. The finding that the daily DDT excretion for lactating women may be slightly greater than the average daily DDT intake of the general population may, at least partly, be accounted for by the fact that during lactation women may eat greater than average amounts of food and/or may mobilize stored

body fat. The constancy of the DDT excretion-level in milk for individual donors over the period of investigation may indicate that the relatively large amount of DDT stored in body fat serves as a 'buffer' to prevent large daily changes in excretion associated with possible daily changes in DDT intake.

Cows' milk also contains DDT; and here, too, as in the case of human milk, the average concentration apparently has decreased over the years. Comparable values for surveys of market milk showed that 67 per cent of samples were positive for one or more pesticides in 1955[12], but only 33 per cent were positive in 1958[13]. Zweig *et al.*[14] have reported that cattle fed a diet containing 0·5 p.p.m. of DDT excreted less than 0·01 p.p.m. of the insecticide in their milk. However, at levels of 1, 2, 3, and 5 p.p.m. of added DDT, detectable residues of DDT, proportional to the level of contamination in the feed, were found in the milk of all animals. The cows fed DDT at the lowest level (0·5 p.p.m.) ate an average of 20 kg feed/day. Thus, their daily dose of DDT was 10 mg/day. Assuming that the average weight of these animals was 400 kg, it may be calculated that the dosage was 0·025 mg/kg/day. This dosage resulted in a DDT concentration of $< 0{\cdot}01$ p.p.m. in the milk of the cows. Even if these cows averaged 0·01 p.p.m. and excreted 15 l. of milk a day, the total DDT excretion in the milk would be 0·15 mg/day or about 1·5 per cent of the dose. Calculations of this sort made for a number of other investigations in which cows have been fed DDT-contaminated diets give results of the same order of magnitude, excretion rates ranging from 1·8 to 29·8 per cent of the daily dose[15]. There seems to be a tendency for a larger fraction of DDT intake to be excreted in the milk at higher dosage rates.

It is interesting to compare these values for the cow with those already given here for women. At a DDT dosage level of about 0·025 mg/kg/day, the cow excretes DDT in milk at a concentration of less than 0·01 p.p.m. and eliminates only about 1·5 per cent of the daily DDT intake in this way. However, at a DDT dosage level of about 0·0005 mg/kg/day, lactating women excrete DDT in milk at a mean concentration of 0·07–0·08 p.p.m. and eliminate about 125 per cent of the estimated average daily DDT intake in this way. Thus, although the calculations for the cow are based on a higher daily intake of DDT, the cow excreted less DDT in the milk both on a concentration basis and calculated as a fraction of daily intake than did lactating women.

Turning now to the question of safety, it appears, from study of available cases of accidental or intentional ingestion of the compound, that the single oral dose of DDT that will cause poisoning in man is about 10 mg/kg[16]. The repeated dose of DDT that is harmful to man is unknown, but studies in volunteers[17,18] and in men with massive occupational exposure[19] show that adults can withstand

without detectable injury 200 times the average dietary level of 0·18 mg/man/day that prevailed in 1953[20]. Furthermore, the general dietary level of DDT has now decreased to about 0·03* (ref. 21) or 0·04 mg/man/day[5]. This amount of DDT corresponds to a mean concentration of about 0·02 p.p.m. DDT in the total wet diet of adults in the United States[5].

The results presented here indicate that babies having human milk as their sole food source are exposed to a somewhat higher dietary concentration of DDT (0·07–0·08 p.p.m.) than is the general population (about 0·02 p.p.m.). Furthermore, the food consumption per unit of body-weight is higher for infants than for adults. If a 5 kg (11 lb.) infant consumed 0·7 l. of milk daily containing DDT at an average concentration of 0·08 p.p.m., the resulting dosage would be 0·0112 mg/kg/day. This value may be compared with the average adult dosage of 0·0005 mg/kg. Also, there is a considerable amount of evidence that young animals, including foetal ones, are somewhat more susceptible than adults to many chemicals including DDT[15]; however, the difference is only a few-fold. On the other hand, there is one report that a single oral dose of DDT was less toxic to young (2·4 h old) than to adult rats[22].

Thus, the information at present available for man indicates that there is, for adults, a large safety factor associated with the use of DDT. For infants, the safety factor appears to be smaller. Continued research and surveillance of the exposed population should be carried out with particular attention being given to the health of infants to ensure that undetected toxic effects do not follow long-continued, low-level exposure to DDT and other persistent pesticides.

* This value was not given in Mills's paper but can be calculated from his data.

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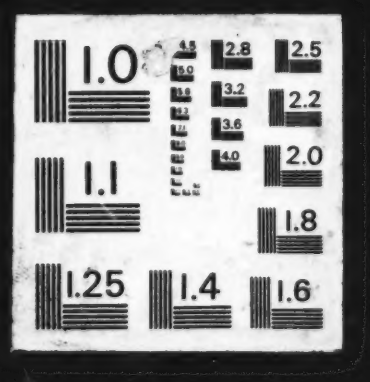

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ORGANOCHLORINE PESTICIDE RESIDUES IN HUMAN ADIPOSE TISSUE

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Persistent pesticides, particularly of the organochlorine type, are currently being scrutinized to determine their potential for causing human or environmental harm. Most uses of DDT were cancelled in June of 1972 by EPA order. The production of the insecticides aldrin and dieldrin was suspended for many uses in October of 1974 by ruling of EPA Administrator Russell E. Train. The insecticide mirex, which is used to control the imported fire ant in large areas of southern United States, is currently the subject of a public fact-finding hearing. A large amount of public awareness and interest is focused on these actions.

The presence and distribution of insecticide residues in human tissue have been among the multitude of factors considered in these regulatory decisions. Most of the human residue data were provided by the EPA National Human Monitoring Program. The purpose of this program is to determine the incidence and level of exposure to pesticides experienced by the general population of the United States and to identify changes and trends in these parameters when they occur. This paper reports findings of selected organochlorine residues for survey conducted on human adipose tissue during fiscal years 1970, 1971, and 1972.

METHODS AND MATERIALS

The program was limited to the collection and chemical analysis of samples of adipose tissue that were obtained with the cooperation of pathologists in 32 cities selected in the contiguous 48 states according to a statistical experimental design.

Sampling A proportionate, stratified-random sampling design was followed for selecting cities in which samples were collected. The population strata were the four census regions as provided by the 1960 Census; the sampling units in each census region were cities with populations in excess of 25,000 people. The number of cities sampled in each census region was based on population distribution. The cities that actually served as collecting sites were selected by randomization (Figure 1).

This design provided samples that would be statistically representative of the pesticide residue levels of the general population. For each collection site, an annual sample quota reflective of the national demographic distribution was established. The number in each of these groups was allocated proportionally according to the age, sex, and race distribution in the 1960 Census.

Adipose tissue was collected by cooperating pathologists and medical examiners from postmortem examinations and from specimens excised surgically for therapeutic reasons.

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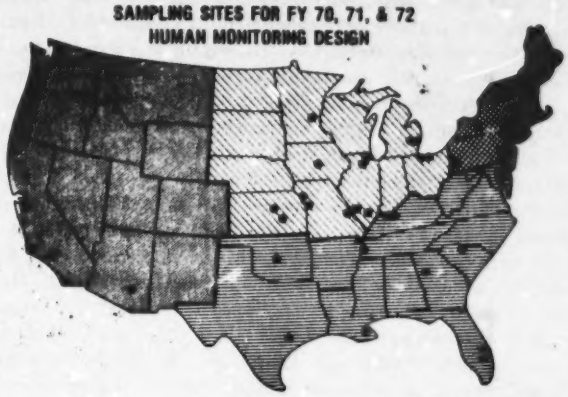
SAMPLING SITES FOR FY 70, 71, & 72
HUMAN MONITORING DESIGN



Thus, tissues were received from patients having pathological conditions as well as those killed by traumatic injury. Information recorded for each tissue sample analyzed included age, sex, race, and pathological diagnosis. Geographic residence was assumed to be in the general location of the hospital. Since the objective of the program was to reflect the pesticide burden in the general population, samples were not collected from cases of known or suspected pesticide poisonings, from cachectic patients, or from patients institutionalized for extended periods. Further details of the program were presented by Yobs (1971).

Chemical Analysis All analyses were conducted by contract laboratories using only methodologies specified by the program. These laboratories were equipped with gas-liquid chromatographs with electron capture detectors. All laboratories were required to maintain acceptable performance levels in the interlaboratory quality assurance program, established and moderated by the EPA Pesticides and Toxic Substances Effects Laboratory. This laboratory also served as technical consultants for the analytical portion of the program.

Samples were analyzed for selected chlorinated hydrocarbon insecticides (Table 1), using a modified Mills-Olney-Gaither procedure (Mills *et al.*, 1963; deFaubert *et al.*, 1964). Thin-layer chromatography was used for confirmation of the results of every fifth sample. Results were reported on a wet-weight basis, and the percent lipid extractable material was included for each sample. The exact analytical methods used in this program were published in manual form by Thompson (1972).

TABLE 1

LIST OF CHEMICALS DETECTABLE IN HUMAN ADIPOSE TISSUE

o,p'-DDT	Aldrin
p,p'-DDT	Dieldrin
o,p'-DDE	Heptachlor
p,p'-DDE	Heptachlor Epoxide
o,p'-DDD	Endrin
p,p'-DDD	Mirex
α-BHC	Oxychlordane
β-BHC	*Trans* Nonachlor
Lindane	Polychlorinated Biphenyls
δ-BHC	Hexachlorobenzene

Computations and Descriptive Statistics. Residue values presented in this paper were calculated on a percent-lipid basis. This conversion was affected by dividing the whole tissue (wet-weight) value by the proportion of lipid extractable material for each specimen. This method of reporting reduced the inherent variation in residue data attributable to differences in the lipid content of individual adipose tissue specimens.

Data were characterized by calculation of several descriptive statistical parameters: sample size or total number of samples analyzed for the particular residue; frequency or percent positive; and geometric mean estimate. In calculating the frequency and the geometric mean, only reports of quantifiable amounts of pesticides were considered; reports of trace amounts were disregarded. Since these residue data tended not to be normally distributed statistically, the geometric mean was adjudged to be the most reliable measure of central tendency.

RESULTS AND DISCUSSION

The residues selected for presentation in this paper were beta-benzene hexachloride, total DDT equivalent, dieldrin, heptachlor epoxide, oxychlordane, and polychlorinated biphenyls. All, except polychlorinated biphenyls, are representative of exposure to organochlorine insecticides; residues of polychlorinated biphenyls are indicative of exposure to that industrial contaminant.

Beta-Benzene Hexachloride (Table 2). This residue was representative of exposure to the insecticide benzene hexachloride. These data showed that this chemical was widely distributed at low levels in the human population during all three years. Although there seemed to be a trend toward reduction in the quantity of residue, this is not reflected in the frequency, which remained equally high during all three years. There has been a hypothesis that certain animals are capable of converting the various isomers of BHC, including lindane, to the beta configuration for storage (Kamada, 1971). If this is true, then storage of the beta isomer may be representative of exposure to all configurations of BHC.

TABLE 2

NATIONAL SUMMARY OF BETA – BENZENE HEXACHLORIDE RESIDUES IN HUMAN ADIPOSE TISSUE

	FY 1970	FY 1971	FY 1972
Sample Size	1412	1616	1916
Frequency	99.15%	99.32%	99.22%
Geometric Mean	0.37 ppm	0.34 ppm	0.23 ppm

Total DDT Equivalent (Table 3). This conglomerate figure reflected the total burden of DDT and its metabolites found in human adipose tissue. DDT had the distinction of being stored in greater amounts than any other organochlorine pesticides found in adipose tissue during these three survey years. Like other residues discussed in this paper, it was found in almost every tissue analyzed.

Biochemically, DDT is dechlorinated in the human body to DDD, and then either metabolized to the water-soluble and excretable DDA, or excreted directly as DDD. DDE storage is not appreciably derived from ingestion of DDT, but rather by ingestion of DDE previously degraded in the environment from DDT. Since DDE is not effectively eliminated from the body, the result is a gradual increase in the body burden of this chemical. On the other hand, DDT would be broken down and excreted more rapidly than DDE (Morgan and Roan, 1970; Roan *et al.*, 1971).

TABLE 3

NATIONAL SUMMARY OF TOTAL DDT EQUIVALENT[1] RESIDUES IN HUMAN ADIPOSE TISSUE

	FY 1970	FY 1971	FY 1972
Sample Size	1412	1616	1916
Frequency	99.93%	99.75%	99.95%
Geometric Mean	7.87 ppm	7.95 ppm	6.88 ppm
Percentage found as DDE	77.15%	79.71%	80.33%

[1]Total DDT equivalent (o,p'-DDT + p,p'-DDT) +1.114 (o,p' DDD + p,p'-DDD + p,p' DDE + o,p' DDE)

Dieldrin (Table 4). Dieldrin residues were reflective of exposure to the insecticides aldrin and dieldrin. Aldrin residues are converted to dieldrin quickly after exposure by the human body. Low levels of dieldrin residues were found in almost every tissue collected. These remained appreciably unchanged during the three collection years.

TABLE 4

NATIONAL SUMMARY OF DIELDRIN RESIDUES IN HUMAN ADIPOSE TISSUE

	FY 1970	FY 1971	FY 1972
Sample Size	1412	1616	1916
Frequency	96.46%	99.20%	98.28%
Geometric Mean	0.18 ppm	0.21 ppm	0.18 ppm

Heptachlor Epoxide (Table 5). Residues of this chemical were representative of exposure to two pesticides, heptachlor and chlordane. Since heptachlor is a component of technical chlordane, we believe that these residues were most reflective of exposure to chlordane. This residue was also found at low levels in most of the tissues submitted to the program.

TABLE 5

NATIONAL SUMMARY OF HEPTACHLOR EPOXIDE RESIDUES IN HUMAN ADIPOSE TISSUE

	FY 1970	FY 1971	FY 1972
Sample Size	1412	1616	1916
Frequency	94.76%	96.23%	90.29%
Geometric Mean	0.09 ppm	0.09 ppm	0.08 ppm

Oxychlordane (Table 6). Oxychlordane is the mammalian metabolite of the chloroisomers of the insecticide chlordane. The capability to detect oxychlordane was introduced into our multi-residue approach during the mid-fiscal year 1971 collection year (Biros and Enos, 1973). Thus, limited data were available for these three years. Based on these figures, oxychlordane was widely distributed at low levels but at high frequencies in humans during this period.

TABLE 6

NATIONAL SUMMARY OF OXYCHLORDANE RESIDUES IN HUMAN ADIPOSE TISSUE

	FY 1971[1]	FY 1972
Sample Size	951	1916
Frequency	93.27%	92.33%
Geometric Mean	0.11 ppm	0.11 ppm

[1]Methodology for detecting oxychlordane in adipose tissue introduced in mid collection year.

Polychlorinated Biphenyls (Table 7). These chemicals are a group of widely used industrial compounds. They are found in many environmental components and, until an accurate analytical methodology was developed, were mistaken for some configurations of DDT (Yobs, 1972).

Analytical methods permitted only the broad categorization of the residue into one of four groups. Slightly less than 75% of the tissues analyzed showed detectable levels of PCB's. Most of the positives were in the 1-3 ppm concentration range.

The National Human Monitoring Program is a continuing function of the Environmental Protection Agency, and reports of more recent surveys are in preparation. As methodologies become available, the scope of the program will be expanded to include additional residues, metabolites, and other evidences of pesticide exposure (Kutz *et al.*, 1974a and 1974b).

TABLE 7

NATIONAL SUMMARY OF POLYCHLORINATED BIPHENYL RESIDUES IN HUMAN ADIPOSE TISSUE

FY 1972 SURVEY

Concentration Range	Number	Percent
Absent	1067	26.01
<1	632	15.46
1-3	2079	50.68
>3	322	7.85

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